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ARCHIVES OF SURGERY

VOLUME 17 NOVEMBER, 1928 NUMBER 5

VENOUS ABNORMALITIES AND ANGIOMAS OF THE BRAIN *

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BALTIMORE

Essentially all lesions common to the blood vascular system are found in the brain. In an article in a recent number of this journal,[1] the arteriovenous aneurysms or fistulas in the brain were analyzed. In this communication, the venous and capillary tumors, aneurysms and abnormalities will be considered. Although the relative frequency of vascular tumors and aneurysms of the brain is difficult to estimate, the actual number is rapidly increasing, owing to the more intensive development of neurosurgery and of the means by which the accurate diagnosis and localization of intracranial lesions can be made. In a series of about 600 verified tumors of the brain, the vascular tumors and aneurysms of the brain (excluding vascular anomalies) were 5 per cent. Eight of these tumors were arteriovenous; fifteen were referable to the venous and capillary system, and seven were arterial.

The vascular lesions most favorable for treatment are those arising from the veins and capillaries. Taken as a whole, they perhaps offer less danger and better results from complete extirpation than tumors of any other type in the brain.

VENOUS ABNORMALITIES IN THE BRAIN

Among a series of cerebral explorations for jacksonian epilepsy, the accompanying seven examples of abnormalities of the venous system were encountered and drawn at the time of operation. In one case, the observations were amplified by necropsy. In every instance, the marked venous irregularities were associated with malformations of the brain, some of which were primary, others secondary.

The venous irregularities were of varied form. In five instances, the sylvian vein was the site of the abnormality. In most of the cases, a number of anomalous veins were spread over the frontal, temporal and parietal lobes and were tributaries to the sylvian vein. It is not an

* From the Johns Hopkins Hospital and University.

1. Dandy: Arteriovenous Aneurysms of the Brain, Arch. Surg. **17**:190 (Aug.) 1928. Since the article on arteriovenous aneurysms of the brain was sent for publication, nine additional probable cases have been found (Blank, Dürck, Federoff and Bagorad, Heitmüller, Herzog, Klimesch, D'Arcy Power, Shoyer, Wichnewski). The references are appended to the bibliography of this paper.

infrequent condition in presumably normal brains for the rolandic vein to be either absent or relatively insignificant, instead of being the outstanding vein of the hemisphere. Such conditions merely indicate the great normal variations of the venous system that occur in the brain and that still appear to be of no significance.

In figure 3 (case 3), one sees a relatively enormous vein over the frontal lobe. This vein is continuous with the sylvian vein as the rolandic vein should be, but it is 4 or 5 cm. anterior to a small rolandic vein which emerges from the brain tissue just below the facial center. In case 5 (fig. 5), the rolandic vein passes from the sylvian as it normally should, but sweeps backward in a crescent, and finally, when approaching the falx, bends sharply forward at a right angle and then again mesially at another right angle. Both of these rolandic variations, however, are only a small part of the composite venous and cerebral abnormalities.

In none of the venous deformities is the size of the vessel abnormal (possibly excepting case 3); rather, it is the number, shape and distribution of the vessels that are abnormal. In this respect the venous changes differ from those of the arteriovenous aneurysms in which the size of the vessels is so striking. In addition to the great size, the venous component of arteriovenous aneurysms also shows great abnormalities in shape, number and distribution. One can always be sure that the lesion cannot be arteriovenous if the veins are of normal size. Moreover, in venous anomalies, aneurysms or tumors, one never sees in the veins exposed at operation pulsating red blood, which is characteristic of arteriovenous aneurysms.

In some instances (fig. 3), the deformation of the cerebral convolutions is even more striking than that of the veins. Many of the convolutions are of relatively enormous size and lack the characteristic shape. They appear like masses of brain tissue, improperly formed. In such cases, doubtless both the veins and the brain tissue are wrapped up in the same fundamental maldevelopment. Case 4 (fig. 4) is another example of a vascular abnormality being dependent on the primary embryonic cerebral defect; the sylvian vein received a branch from each side of the cyst and passed along the sylvian fissure as a bifid trunk. In this case the temporal lobe did not have any attachment to the parietal lobe, except in the depth of the brain.

In case 7 (fig. 7) there was a venous plexus in the sylvian fissure of each side and eight or ten additional small plexuses in the pia-arachnoid over both cerebral hemispheres. In this patient there were two other associated cerebral deformations: (1) absence of the corpus callosum, (2) stricture of the aqueduct of Sylvius with resulting hydrocephalus. The child was an imbecile.

Cerebral and vascular deformations are, therefore, commonly associated. The one may cause the other, or, as in case 5, they may be

entirely independent and referable to a faulty general development in the embryo. In cases 2, 5 and 6, tremendous vascular deformations were present, in that many vessels of fairly uniform size radiated from the sylvian vein. In such cases the vascular bed becomes a space occupying lesion of considerable size and doubtless acts as a tumor, for in each instance the epileptic seizures were focal and began in the face, i.e., the part of the motor area nearest the tumor. Surrounding this vascular bed, there is always a pool of fluid in the subarachnoid space, and usually the leptomeninges over the affected areas are thickened and often opaque. The brain tissue beneath is also softened and the convolutions atrophied as compared with the surrounding unaffected brain tissue. In case 6 (fig. 6) ventriculograms demonstrated that the vascular bed had indented the body of the lateral ventricle. As seen at operation, the network of vessels was so dense that the underlying brain was entirely obscured.

Another abnormality not infrequently seen is the tortuosity of veins. This is shown in a series of anomalous veins in case 1 (fig. 1). Not infrequently one sees many of the smaller terminal veins tortuous when the larger trunks are not affected. In a recent case of a congenitally deformed brain, a series of eight or ten such venules diverged from the center of the frontal lobe, some going to trunks entering the sylvian, rolandic veins, and others to frontal veins passing to the longitudinal sinus. This tortuosity of some of the smaller veins was also present in case 5 (fig. 5). In this case there was also a diverticulum (venous aneurysm of the superior longitudinal sinus).

CLINICAL FEATURES OF VENOUS ABNORMALITIES

With two exceptions (cases 1 and 7) these patients were operated on to find the cause of jacksonian epilepsy. The patient in case 7 was operated on for hydrocephalus; the vascular tumors therefore were incidental. Operation was performed in case 1 because of blindness, and the vascular changes were also incidental. Three of the patients (cases 2, 4 and 7) had varying grades of mental retardation. Another was too young to judge the mental status (case 6).

Two patients (cases 2 and 3) had some slight evidence of motor weakness of the opposite side of the body. In both of these patients the motor weakness was increased for a short time after the epileptic seizures. In one patient (case 5), the epileptic seizures did not begin until he was 28 years old, and in another patient (case 3) the attacks began when he was 13 years of age. The other patients developed convulsions at 5 months, 8 months and 2½ years of age. The time at which convulsions develop from a cerebral lesion is most variable, as these results indicate. The remarkable fact is that a lesion can exist for twenty-eight years without causing trouble and then without apparent reason convulsions will suddenly appear. In arteriovenous aneurysms, the time of onset of attacks may be delayed until much later in life.

Perhaps there is more reason for a later origin in arteriovenous lesions, for they have a definite tendency to increase in size. One can conclude only that any cerebral lesion is always a potential source of epilepsy, and that the time element is uncertain for reasons that are not known.

REPORT OF CASES OF VENOUS ABNORMALITIES OF THE BRAIN

CASE 1.—*Venous Anomaly of the Brain.*

A boy, aged 3½ years, was referred by Dr. Rosenberger of Milwaukee because of blindness. Two weeks before admission to the Johns Hopkins Hospital, the patient had begun to stumble over objects, apparently because he did not see well.

Fig. 1 (case 1).—Field of operation showing the venous anomaly.

He was unable to recognize pictures which he had known perfectly before this time. Since then he had been unable to see at all. There had never been convulsions or any other symptoms. The results of the neurologic examination were entirely negative with the possible exception of the eyegrounds. There seemed to be pallor of the optic disks, though perhaps this was questionable. The x-ray examination of the head was normal,

A suprapituitary tumor was suspected because of the blindness and questionable optic atrophy as suggested by the ophthalmoscopic examination.

The right ventricle was uniformly smaller than the left.

Operation.—Right craniotomy was performed to expose the optic chiasm (fig. 1). A series of four tortuous and somewhat enlarged veins converged from the frontal and parietal lobes to the sylvian vein. Except that the sylvian vein

was larger than usual and bifid for some distance, it was not abnormal. The cisterna chiasmatis was so large that there was a question at the time as to whether this could have caused the blindness. During his stay in the hospital the blindness persisted, but a report two years later stated that his vision was normal again.

Viewed in retrospect, the operative observations did not explain the blindness, nor had the vascular conditions which are here reported caused trouble. They were merely evidences of a congenital maldevelopment in the brain.

CASE 2.—*Venous Anomaly of the Brain.*

A girl, aged 3½ years, was referred by Dr. Walter Cox of Winchester, Va., because of focal epilepsy. Birth had been normal and easy, and had occurred at full term. When the infant was 5 months of age, it had first been noticed that the normal mental response, evidenced by smiling and holding up the head, had not appeared. When she was 8 months old, definite signs of retardation had been noted. When 1 year of age, the right arm and leg had been less developed than the left, and attempts to hold up the head had been unsuccessful. When 18 months old, she had seemed to see things, but did not fix her attention on objects or persons for any length of time. She has never learned to walk or talk. When 2½ years of age, she had had the first convulsion, which had lasted about a minute. The eyes rolled up at the onset of the attack, the right hand drew up, then the leg and soon the entire body was involved in a clonic convulsion. She was unconscious about an hour. Numerous convulsions of similar type had since recurred. On one occasion, six or seven attacks had followed in quick succession. Incontinence of urine and even of feces had been noted. There had been many attacks of petit mal type, evidenced by a momentary staring expression.

Examination.—The child could not stand or talk. She responded with a silly grin when questions were asked. The right side of the body was relatively underdeveloped, though the arm and leg moved freely. There was also slight facial asymmetry. The deep reflexes were increased on the right side.

A probable diagnosis of a congenital lesion of the left cerebral hemisphere was made.

Operation.—Left craniotomy was performed. A large collection of fluid (subarachnoid) covered the anterior half of the exposed area of brain. Over the frontal region, the fluid was at least 1 cm. deep. Through this fluid, and better after its evacuation, five separate interlacing veins (a venous plexus) were seen which filled the sylvian fissure (fig. 2). From this series of veins, twelve or thirteen parallel branches passed across the frontal and parietal lobes to the superior longitudinal sinus. The convolutions of the frontal and parietal lobes were pale, soft, depressed and irregular. The convolutional markings of the temporal lobe were much less affected, but strikingly abnormal also. The subsequent course of the patient was unimproved.

Anatomic Diagnosis.—There was an extensive congenital maldevelopment of the brain. In this, the vascular system shared extensively forming a bed of vessels which almost obscured the frontal lobe.

CASE 3.—*Venous Anomaly of the Brain.*

A boy, aged 14, entered the Johns Hopkins Hospital because of convulsions. Since birth the left side of the body had been smaller and weaker than the right. Mentally, he had been somewhat precocious. One year before admission to the hospital, he had had the first convulsion, which had begun in the left side and which had quickly become generalized. For two years previously, he had had spells of tickling sensation in the left side of the face. No attention had been given to

these attacks, but later they had been an aura of a convulsion. The seizures came on about every two weeks. After a convulsion, the left side was partially paralyzed for several minutes.

Operation.—A right craniotomy was performed on Feb. 19, 1927. The striking observation was the large vein which came out of the posterior part of the frontal lobe about midway between the falx and the sylvian vein (fig. 3). It passed downward into the sylvian vein. A small inconspicuous rolandic vein was about 4 cm. posterior to this anomalous vessel and it had no visible connection with the sylvian vein. The size of the big frontal vein raised the question as to whether an arteriovenous aneurysm might not be beneath, but the blood in the vein was not definitely redder than normal; pulsation could not be seen in the blood stream; nor could a thrill be felt. Even more striking than the venous abnormality was

Fig. 2 (case 2).—Venous and cerebral anomalies.

the great deformation of the convolutions in the frontoparietal region. Several were of enormous size and markedly irregular. Nothing could be done to help the patient. The presence of the old hemiplegia still leads one to wonder if a deep vascular lesion may not be present.

CASE 4.—*Venous Anomaly of the Brain.*

A physician's child, aged 3 years, was mentally backward, unable to raise the head and had frequent convulsions. When 8 months old, he had had convulsive twitchings in the left side of the mouth and face. A month later, there had been a series of generalized convulsions lasting several hours. For the next two years he had had two or three convulsions daily, but for six months before operation they were absent. There has been practically no mental development. For several months he had been getting weaker and had taken food poorly.

When 3 months of age, the patient had had a high fever and a rigid and retracted neck; examination of the spinal fluid revealed 76 cells. Shortly after this attack, his right eye had become crossed, and he had lost the use of his left arm and leg. He had become emaciated and had been unable to move the head for some time. Gradual improvement had followed during the next few months, and the function of the left leg had returned entirely, but the arm had remained spastic and was not used much. It was five months after this illness when the first convulsion developed, beginning in the left side of the face (the affected side).

Physical and neurologic examinations revealed only the slightly spastic left arm which the patient used much less than the right.

The history suggested an old inflammatory lesion, perhaps an old healed abscess.

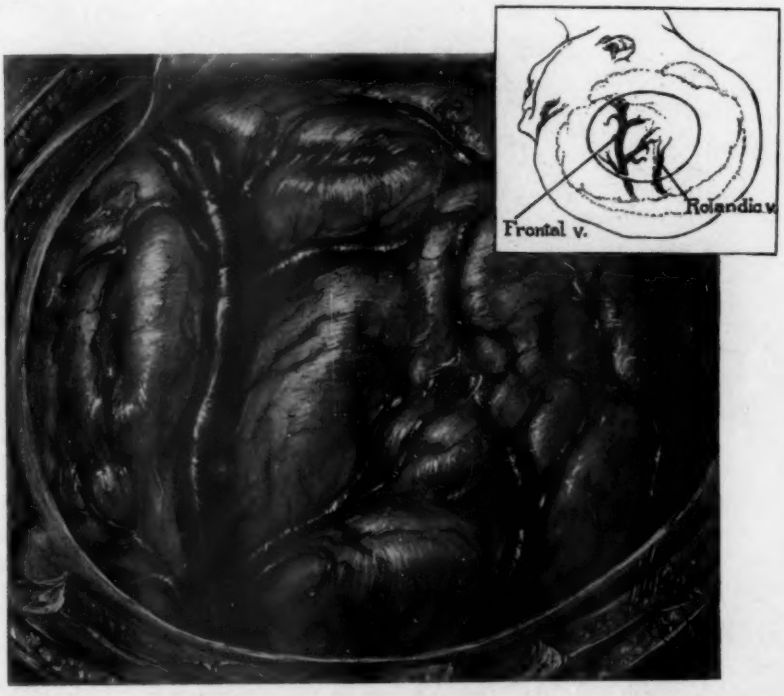

Fig. 3 (case 3).—Venous and cerebral anomalies.

Ventriculography showed a large cavity in the region of the right temporal lobe, filled with air and communicating with the lateral ventricle.

Operation.—The right cerebral hemisphere was explored. A large cyst was found between the temporal and parietal lobes (fig. 4), and opened into the body of the lateral ventricle. A branch of the sylvian vein passed on each side of the cyst. The whole temporal lobe as far back as the occipital lobe did not have any superficial attachment to the rest of the branch. The bifurcated sylvian vein surely represented a congenital malformation. The separation of the temporal lobe from the rest of the brain was surely due to a congenital defect and doubtless the big cyst with its communication with the lateral ventricle was another malformation. There were no signs of an old inflammatory process on

the surface of the brain (adhesions and meningeal thickening). Moreover, if an acute abscess had broken into the ventricle, death undoubtedly would have been the outcome. The failure of the child to develop mentally doubtless denoted other congenital cerebral malformations in the left hemisphere. The child survived the operation, though benefit did not result.

CASE 5.—*Venous Anomaly of the Brain; Also Venous Aneurysm of the Longitudinal Sinus.*

A large, strong miner, aged 29 years, was referred because of jacksonian convulsions. Eight months before admission to the hospital, when picking berries, he had had a severe headache in the left temple. This had lasted a few days, when he had had the first generalized convulsion. There was an aura of pain in the teeth on the right side. He had had nine other major attacks since then,

Fig. 4 (case 4).—Venous and cerebral anomalies. A cyst presenting in the sylvian fissure is responsible for bifid sylvian vein.

in all of which his right hand and face first began to contract. Mental change, dizziness or vomiting was not noted.

The results of the physical and neurologic examinations were entirely negative. The Wassermann reaction of blood was negative.

Operation.—A left craniotomy was performed on March 14, 1928. Aside from two little arachnoid villi which had perforated the dura and formed small knoblike papillomas between the dura and bone (the cause of their formation and their significance, if any, is not clear), nothing abnormal was encountered until the brain was exposed. A striking, congenitally malformed brain was disclosed. The arachnoid was thickened and the subarachnoid fluid formed a large pool over much of the exposed brain. This bed of fluid was particularly deep over a greatly widened sylvian fissure into which nineteen veins of varying size converged from the frontotemporal and parietal lobes. They passed into the sylvian and rolandic veins. The rolandic vein was very large and abnormally placed. It made a big bend posteriorly after leaving the sylvian vein and when about 3 cm. from the

longitudinal sinus suddenly turned forward at right angles, and after a course of 4 or 5 cm. again turned abruptly at right angles to enter the longitudinal sinus. No thrill could be felt in the enlarged rolandic vein, nor was there evidence of red arterial blood in the vessel. Over the frontal lobe another series of veins (about eight in all) converged to three larger trunks which entered the longitudinal sinus anterior to the point of entry of the rolandic vein.

After the subarachnoid fluid had been evacuated, the convolutions were seen to be badly misshapen and malformed. Many were large and pointed instead of having the normal well rounded surface. In addition to these abnormalities, a venous diverticulum from the longitudinal sinus was found with the characteristic anatomic conditions described under the cases of this type. This was removed

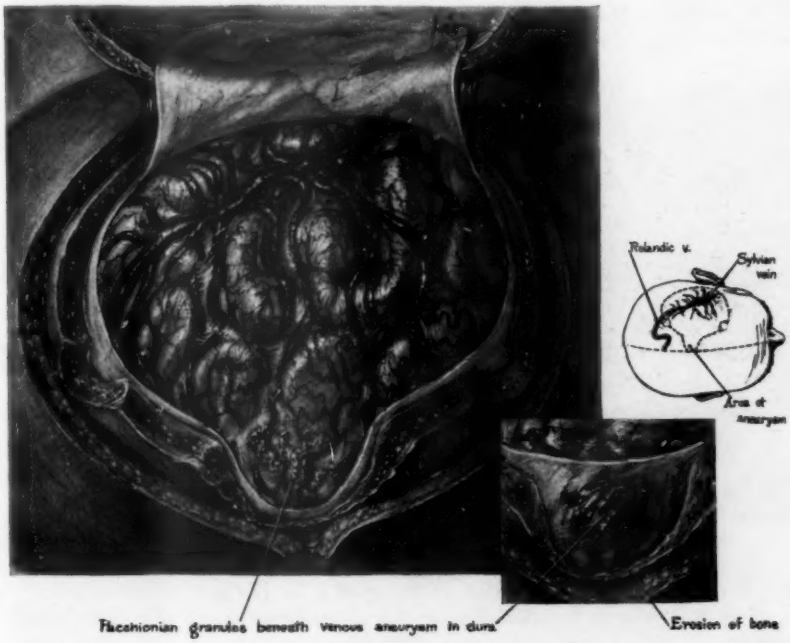

Fig. 5 (case 5).—Drawing at operation, showing masses of veins emptying into the sylvian vein, the abnormal course of the rolandic vein and the venous aneurysm from the longitudinal sinus.

and a fascial transplant sutured in the dural defect. It was not thought that this aneurysm was causing the attacks because they began in the face, but rather that they were caused by the congenital vascular and convolutional ensemble contiguous to the facial center (fig. 5). Nothing could be done to help this.

The postoperative course was uneventful.

CASE 6.—*Venous Anomaly of the Brain.*

An infant, aged 5 months, was referred by Dr. J. W. Amesse, of Denver, because of jacksonian convulsions beginning in the right side of the face but quickly becoming general. The first attacks had begun a month before admission to the hospital. They had steadily increased in number and severity, and many attacks occurred daily.

The results of the physical and neurologic examinations were negative; also the Wassermann reaction of blood. The family history was negative.

Operation.—A small left-sided craniotomy was performed. The sylvian fissure was wide and a roughly circular area extended mesially from it. This area was covered with fluid, beneath which a mass of veins could be seen (fig. 6). After the fluid was evacuated, this cluster of vessels, not unlike a pampiniform plexus of tortuous entwined veins, was more distinct. The vessels completely obscured the underlying brain. They covered Broca's convolution. A second smaller plexus was situated on the temporal lobe about 2 cm. from the large plexus. Several veins bridged the intervening gap and connected the two vascular beds. The vessels were all veins. Palpation did not reveal a thrill nor was pulsation visible. The shape and size of the convolutions were irregular and markedly abnormal.

The operative observations indicated a congenitally malformed brain with venous anomalies.

Fig. 6 (case 6).—Two congenital plexuses of veins in the sylvian fissure. This mass of veins produced an indentation in the body of the lateral ventricle (ventriculogram).

CASE 7.—*Venous Anomalies of the Brain: Venous Plexuses.*

An infant, aged 2½ years, was referred by Dr. J. B. Sidbury of Wilmington, N. C., with the diagnosis of hydrocephalus. The head was large at birth; ptosis of left upper lid also dated from birth. At the age of 3 months, the head had grown rapidly, then measuring 18½ inches (47 cm.). Jerky movements of the extremities had been frequent during the first three months, but there had not been any convulsions. The child had held up her head when she was 6 months of age, and had laughed a month later. She could not sit up alone, though she used her hands and legs in playing. The head did not grow so rapidly after the first six months. At one year of age, it measured 21½ inches (54.6 cm.); at present (2½ years of age) it is only 22½ inches (56.8 cm.). When the child was 5½ months of age, the first tooth had appeared; at 1 year there had been twelve teeth. Her condition had remained more or less stationary for the past eighteen months. She could not sit or stand alone, could not feed herself, and could not

talk. She gritted her teeth a great deal, particularly when she lost her temper. The fontanels were entirely closed. An obstruction in the ventricular system was shown by the fact that phenolsulphonphthalein injected into the spinal canal did not appear in the ventricular fluid.

Operation.—The floor of the third ventricle was removed for hydrocephalus. The fissure of Sylvius contained a venous plexus (angioma). The angioma was made up of cerebral tortuous veins which were entwined. Tributaries converged to the venous plexus from the frontal and parietal lobes.

The child died forty-eight hours after operation. Autopsy showed another venous plexus on the other side of the brain and in precisely the same position, which was almost an exact duplicate of the one found at operation. In addition,

Fig. 7 (case 7).—Congenital plexiform angioma in each sylvian fissure.

there were eight or ten little venous collections of much the same character in the pia-arachnoid membranes over both hemispheres. Each little vascular mass of veins measured from 1 to 2 cm. in diameter, and was flattened on the brain and not elongated like those in the sylvian fissure. They were free in the meninges and could be dissected from the brain. In addition to these vascular abnormalities, the corpus callosum was absent and the aqueduct of sylvius obliterated (figs. 7, 8 and 9).

VENOUS ABNORMALITIES IN THE DURA: VENOUS ANEURYSMS?

In a group of four venous aneurysms with focal epilepsy in which the attacks began in the leg or arm, an anatomatic observation was so uniform and so striking that I venture to suggest an etiologic relationship. The lesion is a diverticulum of the superior longitudinal sinus—a venous aneurysm. My attention was first drawn to this condition in a patient

who had bilateral symmetrical elevation of the skull, to either side of the longitudinal sinus and slightly anterior to the rolandic area. Although superficially the bony prominence suggested an osteoma, the x-ray examination showed this diagnosis to be incorrect, for the bone was

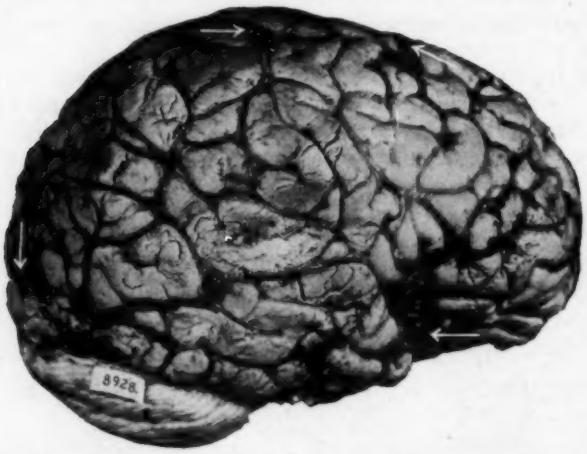

Fig. 8 (case 7).—The venous plexus in the sylvian fissure of the right side of the brain and several small plexiform angiomas over the cortex. The drawing in figure 7 is from the base of the brain.

Fig. 9 (case 7).—Left side of the brain showing plexiform angioma in the left sylvian fissure.

greatly thinned in addition to being pushed definitely outward. On exploration of this part of the skull, the sudden thinning of the bone was found to be striking and the dura immediately beneath to be exceedingly bloody, owing to the presence of a well localized dural vascular bed (fig. 10). On turning back the dura, this same localized area was

found to be densely attached to the brain tissue by pacchionian granulations which were absent both in front of and behind the affected area. Moreover, after the fibrous attachments had been separated the underlying brain tissue was distinctly soft (fig. 11). The palpating finger sank into this part of the brain to a greater depth than elsewhere. There was, therefore, a localized softening of the brain immediately beneath a localized vascular bed in the dura, and a localized erosion of the inner table and bulging of the outer table of the skull directly over the same lesion. It was not difficult to believe that any lesion which could produce such striking changes in the bone could also damage the brain and thereby cause epilepsy. Moreover, its location directly in the prerolandic leg and arm centers suggests the correlation of the pathologic and clinical data.

In excising this vascular dural mass, which bled freely because the dura was thinned and attached to the bone, it could be seen that it was fed by several channels from the longitudinal sinus, and that it did not have a single wide communication with the sinus. There was no arterial communication with the middle meningeal artery, although the bleeding was so severe as to make one wonder if it might not be an arteriovenous aneurysm. It is also worthy of note that the rolandic vein does not enter into this vascular bed in the dura; it passes into the longitudinal sinus, immediately posterior to it.

This patient had only two attacks during the year following the operation and none in the next six years. The capricious results following any form of treatment in cases of epilepsy make any claims hazardous. Moreover, even though the venous aneurysm is removed, the cerebral defect remains and is in itself always a potential source of convulsions. It is, of course, always advisable to remove the primary cause even if the secondary cerebral defect cannot be altered. The attacks will improve even if the patient cannot be cured.

In the two other cases (9 and 10) which I have classified under this group, the clinical and pathologic observations were such exact duplicates of those in the case just described that additional comment is not necessary. Since the operation in these cases has been performed only during the three months prior to the time this paper was written, too little time has elapsed to consider the results. All patients have made uneventful recoveries after removal of the lesion.

There is perhaps reason to deny the existence of this lesion. X-ray examinations of the skull frequently show in this location a degree of rarefaction which must be looked on as a normal observation—usually it is called a venous lake. But in the cases here described, the normal x-ray changes are exaggerated. Where the normal changes end and the pathologic begin must vary in different persons. In fact, in the case just described (case 8), a seemingly identical lesion, and of the same

size, remains on the opposite side and has not caused any symptoms. If the x-ray change is in association with focal convulsions that begin in the leg or arm, and if another lesion in the prerolandic cortex is absent, the existence of the lesion and its causal relationship would seem to be definite.

Brief mention is made of a case in which there was an enormous occipital sinus (case 11, fig. 13). Whether it has any clinical significance is doubtful, but it is an example of a venous anomaly, which may offer great surgical difficulties and dangers if not recognized before it is opened. This sinus, while normally present, may be and not infrequently is entirely absent, and when present its size is most variable, though rarely over 1 cm. wide. In one patient, a hydrocephalic infant, the occipital sinus was proportionately larger than in this patient; it was not the cause of the hydrocephalus but was merely another manifestation of a congenital anomaly. In both of these cases, the occipital sinus bifurcated near the foramen magnum and each branch passed laterally in the dura to enter the internal jugular vein at the jugular foramen.

REPORT OF CASES OF VENOUS ABNORMALITIES IN THE DURA

CASE 8.—*Venous Aneurysm from a Longitudinal Sinus.*

A large, strong man, aged 24, was referred by Dr. W. L. Brown, of El Paso, Texas, in May, 1921, because of recurring jacksonian convulsions. The family and past histories were negative, except for one incident which will be included in the story of his present illness.

The first attack had occurred suddenly six years before admission to the hospital, when the patient was 18 years old. Since that time, they had averaged about two a month, with a tendency gradually to become more severe and more frequent. Every attack came at night just as he was dozing off to sleep. A queer feeling "like a chill" awoke him. In a few seconds the right arm and face began to jerk and then became numb. He then lost the power of speech but was still conscious. He passed into coma as the convulsions became clonic and bilateral. Following the convulsion, he had a queer sulphur taste in his mouth (uncinate attack?). An interesting fact in his history was that when 11 years of age he complained of attacks of numbness of the right arm over a period of nearly a year. This disappeared until the advent of convulsions seven years later.

The results of the physical and neurologic examinations were negative, except for a bony prominence situated in the midsaggital line and extending on each side of the midline; the left side was distinctly a little larger. In the midsaggital plane it was a trifle less than midway between the nasion and the inion. The bony prominence measured about 7 cm. from side to side (bilateral) and 3½ cm. anteroposteriorly. The roentgenograms showed a marked localized bulge of the skull in this region with great thinning of the bone from within.

Operation.—On May 28, 1921, left craniotomy was performed, approaching the midline. The brain appeared normal except for the region of the arm and leg centers where the brain was firmly attached to the dura by a mass of pacchionian granulations. In front of this restricted area which corresponded exactly with the eroded bone in the roentgenogram, the pacchionian granulations and attach-

ments to the dura were absent. The lesion was strikingly localized. The bone was then rongeured away over the affected area. The skull became progressively thinner as the longitudinal sinus was approached, where it was about 3 mm. thick. The denuded dura bled furiously from several perforations of the dura which was closely attached to the area of eroded bone. These venous channels were not continuous with the veins which cross from the cerebral hemisphere and are en route to the longitudinal sinus. Rather they were off-shoots from the longitudinal sinus, and seemed to communicate with a common vascular bed, for it was necessary to ligate all the channels as they entered the longitudinal sinus before the bleeding in the dural vascular bed could be controlled. The rolandic vein passed just posterior to the venous aneurysm to enter the longitudinal sinus. It was not injured. The other interesting feature of the lesion was the firm and dense attachment of the aneurysm to the brain by pacchionian granulations. These had to be severed with a knife or scissors. Contiguous to this local area both anteriorly and posteriorly, these attachments were entirely absent. The leptomeninges were greatly thickened and opaque for some distance beyond the aneurysm and the brain was distinctly softer than the surrounding normal brain. Such observations make it difficult to believe that pacchionian granulations are other than protective formations against the pressure of large venous channels. In the later years of life, the pacchionian granulations develop normally along the rim of brain which lies along the wall of the longitudinal sinus. Doubtless the explanation of these granulations is similarly a reaction to the trauma incident to the flow of blood through the longitudinal sinus.

The entire area of dura containing the venous diverticulum was removed and replaced by a transplant of fascia lata. The dura was divided close to the longitudinal sinus by placing a series of clamps at the base and closing the dural margin with a series of transfixion sutures of silk.

As the convulsions had never primarily attacked the left side of the body, no attempt was made to remove the right-sided lesion, which was a duplicate of that removed from the left.

The immediate postoperative recovery was uneventful. During the first year following operation, the patient had two attacks and has had none in the following six years.

CASE 9.—*Venous Aneurysm from Longitudinal Sinus.*

A highly nervous woman, aged 27, was referred because of frequent jacksonian convulsions. The family and past histories were entirely negative. One year before admission to the hospital, she had suddenly felt dazed for a few seconds (petit mal). Several days later, she had experienced the same sensation. Two or three weeks later, numbness and stiffness had appeared in her right arm and leg in association with the dazed spells. For several seconds after an attack she could not speak or write, and there would be a transient weakness and numbness of the hand and leg. She had not lost consciousness in attacks at this time. In some attacks, the right side of the face twitched. The numb feeling was associated with the sensation of an electric shock passing through the right side of the body. There had not been generalized convulsions. On one day, a few weeks prior to operation, the attacks had come every ten or fifteen minutes. A day seldom passed without the occurrence of severe attacks. Headaches were never present.

The results of the physical and neurologic examinations were entirely negative. X-ray examination showed an area of erosion in exactly the same position as in the preceding cases.

A probable diagnosis of venous aneurysms from the longitudinal sinus was made.

Operation.—On Jan. 24, 1928, a left craniotomy was performed as in the preceding case (figs. 10 and 11). The bone was very thin over a restricted area about as large as a half dollar. The same venous lakes bled freely and had to be controlled by pressure of the finger. The dura was pulled mesially. The same dense area of pacchionian granulations was separated from dense opaque leptomeninges. The same softened zone of brain was immediately beneath. Elsewhere pacchionian granulations could not be seen. A fascial transplant was used to replace the dura which was excised and carefully sutured close to the longitudinal sinus.

The postoperative course was uneventful.

CASE 10.—*Venous Aneurysm from the Longitudinal Sinus.*

A well nourished boy, apparently normal mentally and physically, except for convulsions which began in the right leg, gave a past history which was negative

Fig. 10.—The venous bed connected with the longitudinal sinus. This vascular mass caused both erosion of the skull and indentation of and consequent injury to the brain.

except that glands of the neck had been removed eight years before the present examination. There was no history of epilepsy on either side of the family.

The convulsions began three years before admission to the hospital, when he was 11 years of age. There was no antecedent history of trauma or illness which seemed to have any bearing on the onset of the attacks. From the beginning the seizures were of jacksonian character always beginning in the right leg, and almost simultaneously, but a trifle later, in the right arm. Frequently, a numbness of the right leg and at times of the right arm was an aura. A residual weakness of the right leg and less of the arm followed the attack and persisted for several minutes. The convulsions lasted from one to two minutes, were clonic and became general as consciousness was lost. He had never bitten the tongue or lost sphincter control. There was usually sufficient warning to allow him to sit down before

the attack came on. The attacks became more frequent, averaging about two a month. Most of the convulsions occurred just after wakening in the morning.

The results of the physical and neurologic examinations were entirely negative. There was no objective weakness of the right arm and leg. The roentgenogram showed a marked thinning of the inner table of the skull along the midsaggittal line and about midway between the nasion and inion (fig. 12). The area of erosion was about 3 cm. long. There was a slight bulging of the outer table over this region.

The combination of this erosion of the skull and the focal attacks beginning in the leg suggested that the probable lesion was a venous aneurysm—diverticulum of the longitudinal sinus.

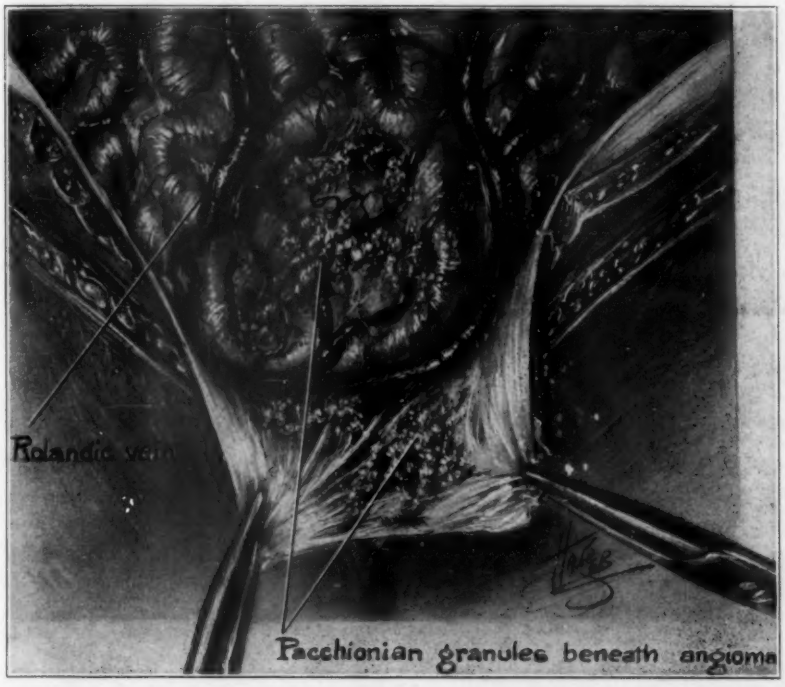

Fig. 11.—Sketch made at operation to show the effect of the dural venous aneurysm on the brain. The under surface of the dura is attached to the brain by a mass of pacchionian granulations.

Operation.—Precisely the same operation was performed and the same observations were disclosed as in the first case of this group.

The immediate postoperative recovery was uneventful. The operation was performed only a month before this paper was written.

CASE 11.—*Abnormality of Occipital Sinus.*

A well nourished man, aged 34, was referred by Dr. W. S. Thayer because of headaches in the occipital region. Throughout boyhood, the patient had had periodical headaches, always localized to the back of the head, at times radiating to the eyes. The headaches had increased with age. They were always intensified by work or exercise, and improved when the patient was in a recumbent position

or by the application of cold to the head. During the past year, the patient had several attacks of weakness and numbness of the left arm and leg, but the motor power was never entirely lost.

The patient's head has been abnormally large since childhood, but has not grown in the past fifteen years. The large head suggested a spontaneously healed hydrocephalus.

The results of the physical, serologic, roentgenologic and neurologic examinations were negative. Two diagnoses were suggested: (1) a cerebellar lesion which might have been responsible for the old hydrocephalus and was now causing attacks affecting the left side of the body; (2) a neurosis. The patient was very introspective, and had always feared paralysis.

Operation.—A cerebellar exploration was made after ventricular estimation had shown large ventricles. An enormous occipital dural sinus 2.5 cm. in width was

Fig. 12.—Erosion of the bone by a venous aneurysm of the dura.

found and ligated (fig. 13). The cerebellar region was normal. The foramen of Magendie was as large as the circumference of a lead pencil. The patient's headaches persist unchanged five years after the operation. The occipital sinus therefore had no bearing on the causation of the headache.

ANGIOMAS

Luschka (1854), who described the first angioma of the brain, divided angiomas into two types: (1) those arising by sequestration of a small portion of the embryonic capillary vascular system; (2) "true tumor" formation from vascular tissue. His case was of the latter type—a true tumor. The first type corresponds to the vascular nevi or telangiectases of the skin.

Before Luschka's report, tumors of both types were well known elsewhere in the body, and because of their cavernous structure Rokitansky referred to them as "cavernous angiomas," a name by which they have since been known. It is questionable whether this classification is pertinent at the present time. There is, it is true, the type in which there is little connective tissue between the vascular spaces, and another type in which the connective tissue predominates and the vascular spaces are of microscopic size; but there seems little, if any, fundamental difference between the two types. Certainly both types grow like tumors. Whether one arises de novo and the other is always of congenital origin has not been proved. At the present time it seems prefer-

Fig. 13 (case 11).—Operative sketch of an occipital sinus of tremendous size. It is a congenital venous anomaly.

able to avoid classification based on conceptions of origin and to group them all as cavernous angiomas. When the stroma is in abundance and the vascular spaces microscopic, this type of angioma is frequently known as hemangiomendothelioma or perithelioma. In addition to cavernous angiomas, there is another type which should be added—venous plexus or angioma plexiforme.

ANGIOMA PLEXIFORME

A lesion of this character has been described among tumors of the spinal cord, where they are not uncommon. In a series of seventy-five tumors of the spinal cord, I had four angiomas of this character. In

a review of the literature on angiomas of the brain, I did not see any reference to similar observations, unless the case of D'Arcy Power is of this type. From the brief note and the accompanying sketch, this appears unlikely; more probably the tumor in Power's case was an arteriovenous aneurysm.

There seems to be no reason why a venous plexus should occur in the spinal cord and not in the brain. In the present series of angiomas of the brain, there are four examples of this lesion. A remarkable example of bilaterally symmetrical venous plexuses in the sylvian fossae is shown in case 7 (figs. 7, 8 and 9), reported under venous anomalies. In addition, there are several smaller circumscribed plexuses over both cerebral hemispheres. This patient was only 2½ years old, and since the vascular lesions were accompanied by other congenital cerebral defects, it is fair to conclude that the angiomas were of congenital origin also. Cases 2 and 6 (figs. 2 and 6) of the venous anomalies are also examples of this lesion, although in case 2 the form was perhaps less pure, since numerous large veins ran into the plexus, making it less sharply defined. These three cases show how insensibly venous anomalies and venous angiomas of this type blend into each other. In a final analysis they are probably identical.

A fourth example (case 12, fig. 14) of this lesion is presented with reservations, since the entire extent of the lesion was not seen. Although the tumor displayed the exact gross appearance of an angioma of the venous plexus type, it is not impossible that an underlying solid tumor may have been beyond operative exposure. Although solid tumors may cause a plexiform assembly of veins, it seems incredible that one so extensive could arise from this source. At the time of the operation, an extensive exposure was made in search of a solid growth. This patient was the only one of the series who was an adult. His symptoms were those of a slowly growing tumor in the hypophyseal region. The sella turcica was destroyed; there was at first bitemporal hemianopsia and later primary atrophy of one optic nerve with retention of vision only in the nasal half of the other eye. There was also, in addition, pain in the trigeminal domain on both sides, probably explainable by the overflow of the angioma laterally. In retrospect, it is difficult to see how the character of the lesion could have been determined from signs and symptoms. One should still have had to be content with the preoperative diagnosis of a hypophyseal tumor.

There has not been any occasion to remove a venous plexus of the brain. In one patient (case 7), it appeared to have no bearing on the hydrocephalus, for which relief was sought. Should one be more favorably situated over the cerebral cortex and at the same time be more circumscribed, it should not be difficult to remove. I have removed completely four of these from the dorsal side of the spinal cord, with

only one death, which occurred several days later from meningitis. Although the hemorrhage might at first appear to be a formidable danger, there is actually little to be feared. The loops of veins are bound loosely with arachnoid connective tissue, and when carefully separated, the whole network of venous loops becomes disengaged, much like a skein of yarn, and becomes resolved into two or three long veins which communicate with each other and with other veins on the surface of the cord. In the case which came to necropsy, the venous channels had entered into the spinal cord. The venous spaces within the spinal cord occupied a considerable volume of the cord and probably accounted for the symptoms more than did the great plexus of vessels on the surface.

REPORT OF CASES OF ANGIOMA PLEXIFORME

CASE 12.—*Angioma Plexiforme.*

A physician, aged 44, was referred by Dr. Carl Henning of Washington with the diagnosis of a hypophyseal tumor. His chief complaints were continuous ocular neuralgia and bitemporal hemianopsia. He had always had headaches. Due to severe paroxysms of pain in the eyes, he had became a morphine addict, finally taking from 10 to 12 grains (0.65 to 0.78 Gm.) a day. The addiction to morphine dated back six years, when the pains had become unbearable. Only through the use of this drug was he able to keep at his work. The pain first began in the right eye and often radiated to the cheek and teeth on the right side. Two years before admission to the hospital, diplopia had appeared and had been present at varying intervals until this report was written. At that time, an x-ray examination showed erosion of the posterior clinoid processes. Two years before, pains of the same character had extended to the left eye, face and teeth. A bilateral temporal hemianopsia had then been found by Dr. Henning. Teeth on both sides had been extracted, at patient's insistence, in an effort to get relief from the pain. Eighteen months before, a subtemporal decompression had been performed elsewhere, but without appreciable benefit.

Neurologic examination revealed the following: 1. A bitemporal hemianopsia was noted which was not sharply demarcated, there being some slight vision in the temporal fields near the center. The visual acuity was greatly reduced, more in the right eye, with which fingers could not be counted at a distance of 20 cm. 2. There was the characteristic pallor of primary atrophy in the temporal side of both disks. The nasal margin of each disk was hazy. The retinal veins were moderately engorged and tortuous. 3. There was complete destruction of the posterior clinoid processes (x-ray examination); the sella turcica was deep. Otherwise, the results of the examination were negative. There was no objective, sensory or motor disturbance referable to either trigeminal nerve. The Wassermann reaction of the blood was negative.

Operation.—In March, 1922, an anterior right craniotomy was performed for exploration of the hypophyseal region. A bluish tumor protruded anteriorly between the optic nerves (fig. 14). When the arachnoid membrane was opened and the cerebrospinal fluid allowed to escape, the tumor was seen to be a mass of entwined veins, each about as large as a slate pencil. Pulsation could not be observed. There was no evidence of arterial blood such as one sees through the wall of distended veins in an arteriovenous aneurysm. Treatment of the lesion being hopeless, the wound was closed. The patient died thirty-six hours after

operation, presumably from restriction of morphine, though possibly from an extradural hemorrhage. He was conscious until shortly before death. Necropsy was not permitted, so that further observations on the origin and distribution of the angioma cannot be added to the operative notes.

CYST WITH ANGIOMA IN THE WALL

Of all the tumors of the vascular system of the brain, angiomatous cysts offer the best prognosis. It may almost be said that as a type and eliminating individual exceptions, they offer more than any other tumor of the brain. Usually the cyst is large and the tumor small. The

Fig. 14 (case 12).—Plexiform angioma in the region of the hypophysis. It caused all the symptoms of a hypophyseal tumor.

tumor is embedded in and projects from some point in the wall of the cyst. Always relatively small, compared to other tumors, it may actually be so small as to escape casual observation. There can be no doubt that in many of the so-called simple cysts a tiny angioma will be found on more careful inspection. The solid tumor is flat or rounded; it varies in size from a few millimeters to 2 or 3 cm. in diameter. Its surface is smooth and appears to be covered by the smooth lining of the cyst, but the cyst is not lined with epithelium. On sectioning the wall, a minute, insignificant looking, reddish brown lesion will frequently be

found to cause the relatively enormous cyst. In the gross appearance, the intracystic angiomas are usually mistaken for gliomas. A careful gross inspection will usually make the differential diagnosis. An angioma is fibrous and acellular and the larger tumors are usually compressible and spongelike. In the fixed specimen, the tumor has changed from reddish brown to black, because of the old fixed blood in the tumor. A glioma is softer, more cellular and consequently more friable. Cells of the latter easily scrape off on the edge of a scalpel. It is noncompressible and its color a more uniform brown in the fresh specimen and a less intense brown or black when fixed. The content of cysts, whether of angiomatous or of gliomatous origin, is apparently the same. In either type, the fluid is clear lemon or orange yellow and a white coagulum is present at the bottom of the cyst. The reason for the cyst formation in these tumors is not known.

In an intensive study of cysts of the cerebellum, Lindau assembled fifteen cases, including a case reported previously by Schloffer, and another by Friedrich and Stiehler. This number is many more than the combined total number of all the cases, both cerebral and cerebellar, in the literature.

Other cases of angiomatous cysts were reported by Luzzatto, Bielschowsky, Baum, Bruns, Koch, Newmark and Schweyer. Four of these (Bielschowsky, Baum, Bruns and Schweyer) were in the cerebral hemispheres; two in the cerebellum and one (Luzzatto) in the brain stem. Koch's patient had bilateral angiomas. In Newmark's case, the tumor was in the meninges and the cyst was extracerebellar. Including my seven cases, there have now been reported twenty-nine cases of angiomatous cysts, twenty-four cerebellar, four cerebral, and one in the brain stem.

It is of interest to note that Lindau found angiomatous cysts to be almost twice as frequent as those of gliomatous origin. He doubtless refers to the large cysts with small single intracystic papilloma. Lindau's statements are supported by careful histologic studies with differential stains to detect glia fibers. From operative experience, the histologic evidence indicates the angiomatous and gliomatous cysts to be about equally divided. However, there are three cases diagnosed gliomatous cysts which I feel confident, because of the gross description in the operative notes, are angiomatous cysts; the sections have been lost. If these are really angiomatous cysts, the results would be similar to those of Lindau. On a restudy of the histologic material, it is surprising to find how many tumors have previously been diagnosed gliomas when they are sharply defined angiomas. There are many exceedingly vascular gliomas which in the gross or microscopic examinations might be mistaken for angiomas, but a careful study of the vascular spaces of a glioma show well defined vascular coats which are absent in the

angioma. Moreover, even with a hematoxylin eosin stain, the reticulated stroma of a glioma has little resemblance to that of an angioma.

Lindau's intensive study demonstrates anew the fact that when supposedly rare lesions are better known they are frequently found to be common. All seven of my cases of intracystic angiomas were in the cerebellum. As indicated in the accompanying sketches, the solid tumors were located at divergent parts of the wall of the cyst. All have reached the surface of the cerebellum and have been in contact with the pial vessels, but whether this is significant in their origin, I am not prepared to suggest.

Clinical Features.—There is nothing characteristic about the signs and symptoms produced by angiomatous cysts. Other types of cysts in the same position and of the same size give identically the same disturbances. All produce intracranial pressure, usually but not invariably evidenced by headache, nausea, vomiting and papilledema; they therefore compromise life. In most instances they also induce symptoms of localization, but this is not always true. If the cyst occupies a silent area of the cerebral hemisphere, localizing symptoms will be absent until it has grown alongside cerebral tracts with function—speech, motor, sensory, visual, uncinate, etc. All of the cases of cerebellar cysts collected from the literature showed outspoken so-called cerebellar disturbances—staggering gait, often with the tendency to swerve to one side, positive Romberg sign, and often nystagmus, ataxia, adiadokokinesis, stiffness of the neck and dizziness. One of my patients did not have any symptoms or signs of localizing import. Another had symptoms which were suggestive, but not positive. In these cases, ventriculography and ventricular estimation made the location absolute.

Clonic convulsions probably never occur with cerebellar cysts, but frequently with cerebral cysts. Convulsions resulting from cerebral cysts are often of focal character and may have the jacksonian characteristics. In the cerebral cases reported, in those of Schweyer, Bruns and Baum the patients had jacksonian seizures; Bielschowsky's patient alone did not have convulsions. None of the twenty-four cerebellar cysts produced clonic convulsions. On the other hand, tonic spasms may occur in the late stages of cerebellar cysts. Such attacks are, in fact, characteristic of a tumor in the posterior cranial fossa; they result from compression of the motor tracts in the brain stem. This phenomenon was seen in cases 14 and 15. Newmark's patient had momentary losses of consciousness without convulsions.

Although a genuine hemiplegia or hemianesthesia is usually referable to lesions of the cerebral hemisphere, a few of the cerebellar angiomatous cysts induced paralyses, though usually in transient attacks. One of Lindau's patients had attacks in which both legs were paralyzed; another lost the use of the left arm and leg at times. Two of my patients had

attacks of pain and numbness in one side of the body (cases 13 and 18). One of Lindau's patients and one of mine had trigeminal pain; in both instances the cerebellar cysts were unilateral. Luzzatto's case of a cyst in the medulla gave symptoms suggesting syringomyelia, and in its gross appearance the cystic cavity was like that found in syringomyelia. Recently several cases of syringomyelia with cysts of the spinal cord have been reported in which tiny angiomas have been secreted in the walls of the cysts.

The reflexes are altered according to the relationship of the tumor to and the degree of injury of the motor tracts. Among the cerebellar cysts, reflex changes are usually not great, though not infrequently ankle clonus, a positive Babinksi reflex and increased deep reflexes are present on one or both sides—constantly or transiently. The corneal reflex is frequently diminished and at times absent on the side of the unilateral tumor and on both sides from a midline tumor of the cerebellum.

The age at which symptoms first appear is essentially the age of greatest frequency of tumors of the brain in general, i.e., between the ages of 25 and 50.

The time of the initial symptoms in eighteen cases of cerebellar angiomatous cysts is as follows: between the ages of 20 and 30, three cases; between 30 and 40, nine cases; between 40 and 50, four cases; between 50 and 60, two cases.

In half of all the cases, symptoms first appeared in the third decade. The youngest patient was 21, the oldest, 52 years.

The duration of symptoms before death or operation is surprisingly short in most cases of cerebellar cysts. In six, the symptoms had been present less than six months; in four, less than one year or more than six months; in four, two years or less; and in one each, three, four, five and eight years. In approximately half of the cases, therefore, the symptoms began less than one year before death or operation. Only two cerebral angiomatous cysts have data concerning the duration of symptoms; Bielschowsky's patient had symptoms for fourteen months and Schweyer's for twelve years. It is obvious that the rapid onset of symptoms is due, not to the size of the comparatively insignificant tumor, but to the growth of the cyst which forms with relatively great rapidity.

Four of my patients were males and three were females. From the cases in the literature there are more males, fifteen to eleven. The frequency is probably not influenced by sex.

By using this analysis of signs and symptoms, it appears possible to make at least a tentative diagnosis of an angiomatous cyst—an absolute diagnosis seems impossible. Given a cerebellar tumor appearing in a patient between the ages of 25 and 40, symptoms rapidly progressive (less than one year) with variations in them from time to time and the

absence of profound disturbances of a primary lesion of the brain stem a cyst, angiomatous or gliomatous, should be suspected.

Treatment of Patients with Angiomatous Cysts.—Angiomatous cysts are usually among the easiest and safest intracranial lesions to extirpate. Extirpation of the little tumor embedded in the wall of the cyst is sufficient. The extirpation must be done painstakingly, and a good margin of tissue must be included with the angioma. The danger is minimal when the tumor is small and situated near the surface. It increases somewhat when the tumor is larger and is located far forward over the midbrain. The larger tumors are usually vascular and for this reason offer difficulties in removal. A most important factor in the safety of the operation lies in the early diagnosis. In the late stages, the subtentorial pressure is so high that the dura cannot be safely opened because the cerebellum will herniate through the dural defect and rupture. Puncture of a lateral ventricle will relieve the supratentorial pressure, but not enough to prevent injury to the cerebellum. Puncture of a cerebellar lobe with a hollow, blunt needle will eliminate this hazard when a cyst is reached.

It is hardly necessary to add that as methods of treatment in an effort to cure tapping or completely evacuating a cyst by a transcortical incision, or treatment of the tumor by Zenker's solution or some other fixative are perfectly futile. They are inexcusable, for they have left uncured a lesion which can be so easily removed and permanently cured.

The operative efforts reported in the cases compiled from the literature have not been numerous. The first extirpation of a tumor of this type was performed by Bruns in 1897, but his patient died of meningitis. Baum's (1911) patient was in coma at the time of the operation, recovered, and died a year later of pneumonia. Schloffer's (1926) patient recovered after an extensive resection of a cerebellar hemisphere. One of my patients died nearly ten years ago, without exposure of the tumor. At that time there was no means of locating the tumor (she was in deep coma at the time) and the then routine subtemporal decompression was performed, of course, without relief. From careful inspection of the autopsy specimen, it is doubtful whether at that time the cyst could have been found for there was no surface evidence of its presence when the brain was removed. The tumor was 4 cm. beneath the surface of the cerebellum. I have also wondered whether the solid part of the tumor would have been detected had it been possible to locate and open the cyst. At the present time, however, the methods of accurate localization of tumors would make the disclosure of the cyst possible regardless of its depth. The five patients on whom the extirpation of the tumor in the wall of the cyst has been performed have made uneventful and complete recoveries and are now living and well. They are without any signs of recurrence of the tumor. One patient is well seven years

after operation (April 13, 1921). At the time of the operation, he was in deep coma. The operation was performed only after the tumor was localized by ventriculography. Another patient is well after five years. Her vision, which was lost due to retinal hemorrhages caused by the intracranial pressure, has returned to normal. Another patient who was nearly comatose quickly became conscious after operation (sixteen months ago).

The seventh patient died en route to the hospital, though in good condition when he left home. The sudden development of coma, and the comparatively short duration of the intracranial signs and symptoms, make an early diagnosis of paramount importance, if cures are to be obtained. Often warning is not given that death impends.

The only safe way to relieve intracranial pressure due to a cerebellar cyst is to evacuate the cyst. The relief is then prompt and complete for the time being; it becomes permanent when the tumor—the cause of the cyst—is removed. The evacuation of the cyst relieves not only the direct pressure on the brain stem, but also the hydrocephalus. Relief of the latter is almost as important as the former, for the hydrocephalic ventricles gradually push the tentorium backward and exert great pressure on the structures—including the medulla—in the posterior cranial fossa. A subtemporal decompression does not effect relief in the slightest degree. A subtentorial decompression may or may not effect temporary relief depending on whether the tumor can be lifted from the foramina of Luschka. The only safe and certain attack therefore is to open the cyst and extirpate the tumor. This same principle of relief by the direct operative attack on tumors holds true for all intracranial neoplasms. There could not be better proof of this statement than the prompt recovery from coma after removal of the cause of the intracranial pressure in the foregoing cases.

REPORT OF CASES OF CYST WITH ANGIOMA IN THE WALL

CASE 13.—*Angiomatous Cyst.*

A well nourished woman, aged 32, blind and unable to stand, was referred by Dr. George Price of Spokane, Wash. Her symptoms dated back only seven months, when she had noticed stablike pains in both eyes which had lasted only a few seconds and had disappeared when she lay down. There was also some headache in the frontal region and sides of the head. They had become more severe and more persistent; for the two months prior to operation they were constant.

Sudden fainting spells, lasting from ten to fifteen minutes, and without loss of consciousness, had occurred nearly once a week for the past five months before operation. She felt dizzy during these spells; her "thoughts were paralyzed" and "everything seemed to rush to the head" and she would fall to the floor. Staggering gait had been present two months; she swayed from side to side and had a tendency to bear to the right. She had had occasional attacks of numbness of the right arm and leg, and the neck had been rigid.

One month before admission to the hospital, her vision suddenly had become blurred and since that time she had been blind. Attacks of nausea and vomiting had been present for the past three months. It is of interest that two years ago an ovarian tumor, said to be a carcinoma, had been removed by Dr. Terry in San Francisco.

Neurologic examination elicited the following positive observations: 1. There were tremendous bilateral choked disk (6 diopters); each nerve head was covered with dozens of hemorrhages. Much of the contiguous retina was also obscured by the hemorrhages. 2. The patient could not see fingers with either eye. 3. She showed a positive Romberg sign and fell to the right. 4. Staggering gait and

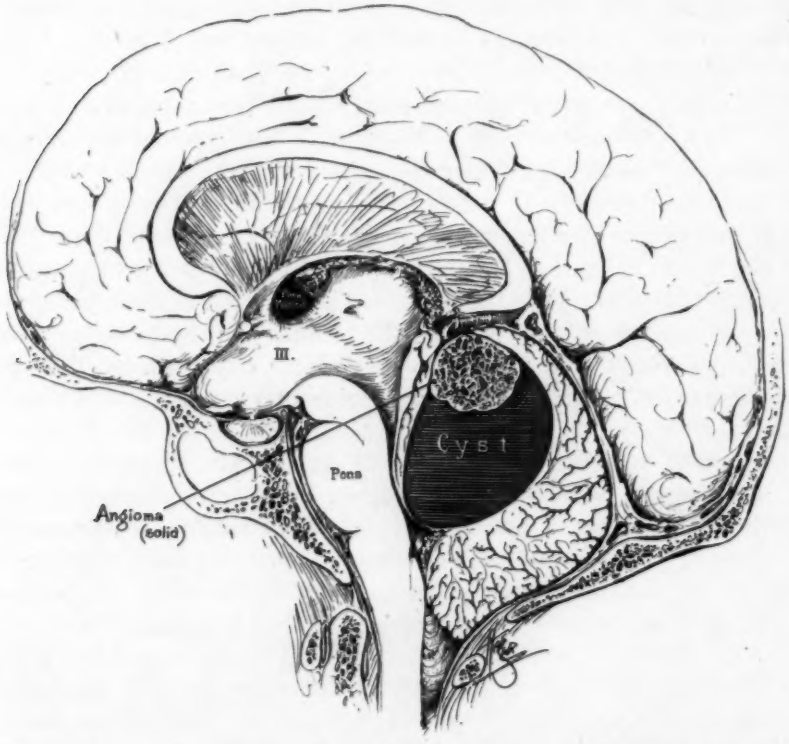

Fig. 15 (case 13).—The operative observations in an angiomatous cyst. The solid tumor was situated directly over the midbrain.

5. Hyperactive but symmetrical reflexes were present. The Wassermann reaction of the blood was negative. X-ray examination of the head was negative. A metastatic tumor was suspected.

Ventricular estimation (at time of operation) showed that the lateral ventricles were large and communicated freely with each other (indigo carmine test). The pressure of the ventricular fluid was very high.

Operation.—On Jan. 6, 1923, cerebellar exploration was performed. A large cyst was struck with a hollow needle 3 cm. below the surface of the vermis (fig. 15). A transverse transcortical incision was then carried into the cyst, which was larger than a walnut. Straw colored fluid escaped, and a gelatinous coagulum

was removed. A small, rounded, firm papilloma about the size of a hazelnut projected from the wall of the cyst at its anteriormost part and lay just under the great vein of Galen. Its removal was attended by such profuse bleeding that its angiomatous character was at once apparent. Though its base was only about 0.75 by 0.75 cm., every attempt to dissect it free was followed by a brisk hemorrhage. After it was removed the bleeding surface was temporarily packed with moist cotton under pressure, and later the use of silver clips completely stopped the bleeding. The unopened fourth ventricle bulged into the floor of the cyst.

Microscopic examination showed that the tumor was made up of endothelial lined, blood-containing spaces of varying size. Abundant connective tissue interposed between the vascular sinuses was the only other feature of the tumor.

The patient made an uneventful recovery. Five years later, she was well; her vision had returned; her gait was unaffected, and she was able to do her own housework.

CASE 14.—*Angiomatous Cyst.*

A poorly nourished woman, aged 36, was referred by Dr. F. H. Kliefoth, of Schertz, Tex., on Feb. 20, 1928. Six months before, suboccipital headaches had first appeared with nausea and vomiting. Dizziness and staggering gait, dimness

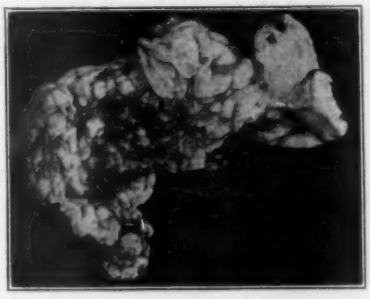

Fig. 16 (case 14).—Small mass of cerebellar tissue removed with the angioma. The light part of the picture is cerebellar tissue; the dark area is the angioma.

of vision and diplopia had soon developed and had increased. Later, the patient had been subject to "nervous spells" in which numbness extended upward from the fingers and toes of both sides. During these spells, which lasted from twenty to thirty minutes, the arms were flexed, the legs extended and she was unable to move. Until the attack passed, she was unable to speak, although she was conscious.

Examination showed an extremely ill woman. She was drowsy in spite of the severe headaches to which she had been subject. It was evident that she was bordering on coma.

The Romberg sign was positive; she promptly fell to the left; ataxia and adiadokokinesia were positive on the left; there was lateral nystagmus. High grade papilledema of both eyegrounds was observed.

Operation.—The diagnosis of a cerebellar tumor was confirmed by ventricular estimation, and a bilateral cerebellar exploration made. A cyst of the left cerebellar lobe was found and evacuated (fig. 16). The cyst was about as large as a walnut, and contained clear orange-yellow fluid. The fourth ventricle bulged into the mesial side of the cyst. A small smooth reddish-brown tumor, about as large as a split pea, could be seen in the wall of the cyst; it was located in the left cerebellar

tonsil which had herniated into the foramen magnum. It was necessary to liberate the tonsil in order to reach the tumor and permit its extirpation. The tumor was excised with a zone of normal cerebellar tissue on all sides. Histologically, the tumor was a typical cavernous angioma.

The patient made a complete recovery and is now well. There are no residual cerebellar symptoms.

CASE 15.—*Angiomatous Cyst.*

A well nourished woman, aged 44, entered the hospital in coma, in October, 1918. For two months she had complained of dizziness after exertion, and some suboccipital headaches associated with vomiting nearly every day. At first, when perfectly quiet she had been comparatively free from both headache and dizziness, but gradually the headaches had become much more intense and were not affected by resting. She staggered like a drunken person and had shaking of both hands (but more the right), so that at times she was scarcely able to lift the cup to her mouth. She had several attacks in which her whole body became rigid like a board, but consciousness was not lost nor were there any clonic convulsive movements. A month prior to operation, she had had periods of mental cloudiness, some hallucinations and had been disoriented. Later she had alternately laughed and cried and had ceased to take interest in her surroundings.

The physical and neurologic examination showed the following:

A coarse tremor of the right hand and arm was frequently observed. The veins of the forehead and eyelids were very full. The eyegrounds showed fulness of the veins and a beginning bilateral papilledema. The Babinski reflex was positive on both sides; the corneal reflex and knee jerks were normal, and ankle clonus was not noted.

At the time this patient was seen, the stereotyped treatment for such patients was a subtemporal decompression—now known to be useless. Through the operative defect a large lateral ventricle was tapped, reducing the supratentorial pressure to normal. She died twenty-four hours after the operation.

When the brain was examined at necropsy, evidence of the tumor was not found on the surface of the brain. Section of the cerebellum, at a later date, showed a cyst about 3 by 3 cm. in diameter. At first evidence of a solid tumor was not present, but later a small circular thickened area about 3 mm. in diameter was detected. Microscopic examination of this area showed a typical angioma.

CASE 16.—*Angiomatous Cyst.*

A young engineer, aged 28, was seen, in consultation with Drs. Julius and Harry Friedenwald of Baltimore, at another hospital on April 13, 1921. He was then comatose despite a subtemporal decompression which had been performed two weeks before.

The following history was obtained from Dr. Friedenwald: The symptom of onset was an attack of headache, lasting three or four hours, and beginning six months before admission to the hospital. At first, the attack recurred about every ten days, but for the three months before admission they had been continuous and frequently associated with nausea and vomiting. For three months he had been troubled with dizziness and staggering gait. The dizziness was always worse when he was lying on the right side. Diplopia had been present at times for three or four months.

The results of the neurologic examination were negative, except for a bilateral papilledema of high grade. The decompression in the right subtemporal region was full and tight.

Operation.—On April 13, 1921, an injection of air was made; the tumor was localized to the posterior cranial fossa, and a cerebellar operation was performed.

A large cyst of the left lobe was first tapped, then evacuated through a transcortical incision. Clear, yellowish fluid escaped from the cyst. On the posterior lateral wall of the cyst was a smooth, reddish-brown solid tumor about as large as a pea. It reached the surface of the cerebellum. The solid tumor was removed with a zone of normal cerebellar tissue.

Recovery was prompt and complete. The patient has since carried on his occupation and has remained entirely well.

CASE 17.—*Angiomatous Cyst.*

A poorly nourished man, aged 35, was referred with the diagnosis of a tumor of the brain on June 3, 1924. His symptoms dated back only three months, when he had suddenly been seized with a severe occipital headache, dizziness and vomiting. The attack had lasted two days. Similar attacks had recurred with increasing frequency. Three weeks after the onset of his illness, staggering gait had developed. Vomiting had become so intense that he lost 30 pounds (13.6 Kg.) in weight. Occasionally, there had been roaring in the right ear. From time to time, dark spots had appeared before the eyes, and for six weeks before operation his vision had been blurred. He had been bedfast for four weeks fearful of turning his head because of the certainty of precipitating dizziness. Diplopia had not been present.

Neurologic Examination.—The patient could only see enough to count fingers. There was a marked papilledema of both optic nerves. Many hemorrhages obscured the region of the disks. There was a positive Romberg sign, with tendency to fall to the left and backward; retropulsion, unsteady gait, cervical rigidity and ataxia were present. The reflexes were normal. A Babinski reflex or ankle clonus was not noted.

Operation.—On June 4, 1924, ventricular estimation showed marked hydrocephalus, with free communication between the lateral ventricles—indigo carmine passed quickly from one ventricle to the other.

Because of the patient's poor physical condition, the operation was performed under local anesthesia. A large cerebellar cyst was tapped in the left lobe; clear lemon-yellow fluid escaped. A smooth, reddish tumor, as large as a cherry, protruded slightly into the cavity of the cyst at the outer aspect near the midline. It also penetrated through the remaining cerebellar tissue to reach the surface. The tumor was easily excised with contiguous cerebellar tissue. The patient made an uneventful recovery, and has since been well (nearly four years).

CASE 18.—*Angiomatous Cyst.*

A large, strong man, aged 34, was referred by Dr. Malcolm Campbell, of Malvern, Ia., on Oct. 20, 1927, with the diagnosis of a tumor of the brain. His symptoms had begun two years before, when he had first noticed pain in and behind both eyes and radiating to the occipital region. Eighteen months later, severe occipital headaches had begun, and had persisted up to the time of operation. During the month before operation, he had had spells of numbness and tingling in the right arm and leg. Dizziness, vomiting or unsteadiness of gait were not noted.

The neurologic examination showed a bilateral papilledema measuring 5 diopters in each eye. There were no other positive neurologic observations. The Romberg sign was negative; ataxia, or nystagmus was not noted. There were no signs by which the localization of the tumor could be made.

Ventriculography showed that the lateral ventricles were much enlarged; they communicated freely; the third ventricle was enlarged and mesially placed; the aqueduct of Sylvius was patent throughout and also the fourth ventricle until an

abrupt vertical line was reached 2 cm. back of the aqueduct (fig. 17). This line marked the anteriormost part of the tumor.

Operation.—On Nov. 2, 1927, a bilateral cerebellar exposure was made. The bone was exceedingly bloody, despite the release of pressure by a ventricular puncture. The dura was still so tight that it seemed unsafe to expose the cerebellum. Puncture of the left and right cerebellar lobes yielded nothing; on puncturing the vermis, a yellow fluid spurted. With the dural tension relieved, the dura was evacuated. A colorless, gelatinous clot was pulled out of the bottom of the cyst. The outer surface of the cyst contained only meninges, the cortex having been entirely atrophied. The cerebellar tonsils were herniated far into the spinal canal. After the cyst was evacuated, the tonsils could readily be with-

Fig. 17 (case 18).—Ventriculogram showing the localization of an angiomatous cyst which did not give signs or symptoms by which its position could be identified. The wide aqueduct of Sylvius and the anterior part of the fourth ventricle are between the two sets of arrows. The tumor produced an abrupt ending of this ventricular shadow.

drawn from their incarcerated position; as they were withdrawn, one could see a cluster of little yellowish cystic nodules much like a bunch of grapes. They occurred as much in one tonsil as in the other. They were attached to the meninges. The fourth ventricle bulged into the cyst. The anterior part of the solid tumor was attached to the wall of the cyst, where it was inseparable from the fourth ventricle. The entire solid tumor was removed with a good margin of cerebellar tissue. This procedure necessitated the removal of both tonsils and part of the roof of the fourth ventricle. The tumor and brain tissue weighed 9 Gm.

The postoperative course was uneventful. The patient is now well (six months after the operation).

CASE 19.—A man of about 40 years of age was referred by Dr. R. R. Snowden, of Pittsburgh, with the diagnosis of an unlocalized tumor of the brain. For about a year he had been having headaches, which had gradually increased in intensity.

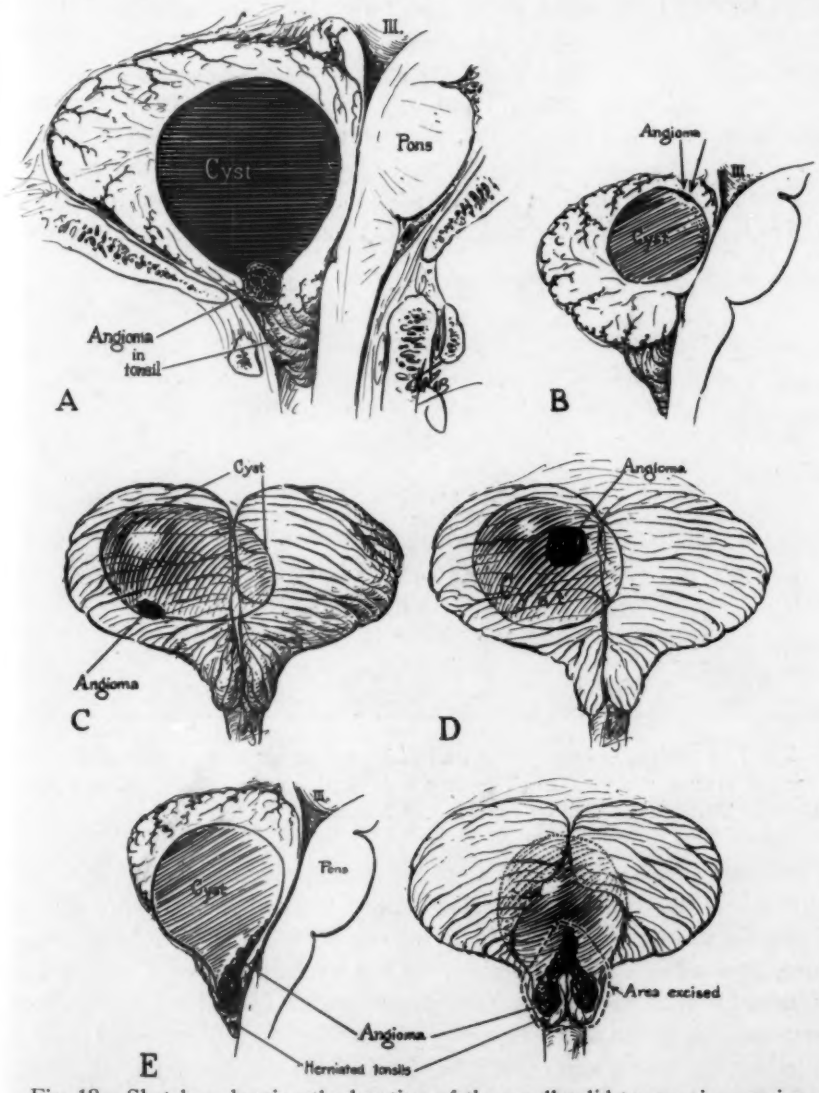

Fig. 18.—Sketches showing the location of the small solid tumors in a series of cysts: (*a*) case 14; (*b*) case 15; (*c*) case 16; (*d*) case 17, and (*e*) case 18.

For a few months prior to death they had been almost continuous. He had loss of vision, hiccups, projectile vomiting and inability to maintain his balance. With the exception of a double papilledema, Dr. Snowden did not make any positive observations on examination.

The patient died en route from the station to the hospital.

Necropsy showed a large cyst of the left cerebellar lobe with a small flat circumscribed tumor embedded in the cerebellum and wall of the cyst (fig. 19).

Microscopically, the tumor was a typical cavernous angioma.

CAVERNOUS ANGIOMA

Cavernous angiomas differ from the foregoing group of tumors principally in the absence of a cyst and in the larger size of the vascular spaces which are usually on the range of unaided vision. The five cases here reported differ greatly from each other in the gross appearance of the tumors. On one extreme, they seem to fuse insensibly with the angiomas associated with cysts, and on the other with the plexiform angiomas. In general, it may be added that they lack the hyperplastic character of the former and the gross venous make-up of the latter.

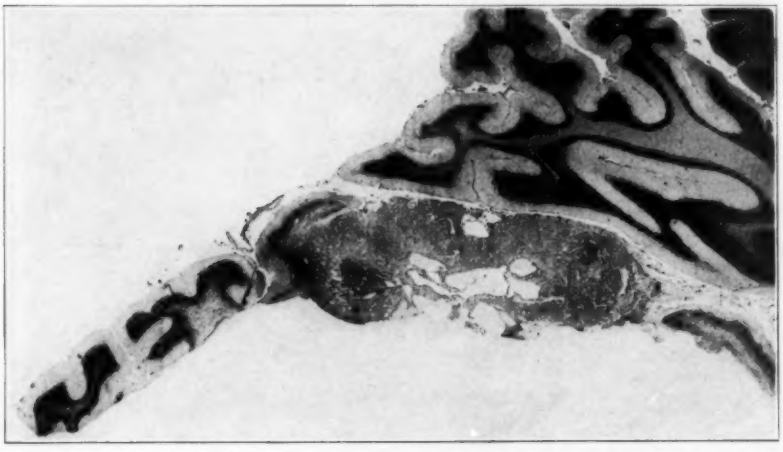

Fig. 19 (case 19).—Angioma in wall of cyst of cerebellum. Some of the larger vascular spaces are visible. The tumor is well circumscribed but not encapsulated. This patient died en route to the hospital.

The tumor in case 20 showed a gross cavernous character, and in case 23, hyperplastic stroma. It has already been noted that the angioma plexiforme fused insensibly with the venous anomalies. It would seem therefore, that other types of lesions of the venous and capillary systems blend with each other. Perhaps it may be preferable to subdivide the cavernous angiomas into two types according to the early proposal of Luschka, but for the present I am inclined to disregard the differences and group them all together. Although many of the lesions of both the embryonal vascular type and of the angioplastic type (the so-called "true tumor" of Luschka) are small and apparently dormant, others with seemingly the same histologic and gross appearance are undoubtedly growing. Either, therefore, may or may not act as a neoplasm. Prob-

ably the most rapidly growing and much the largest tumor of my series was one of the primitive vascular—presumably the least active—type.

Until Lindau's publication, the overwhelming percentage of angiomas was cavernous. With the addition of his great number of angiomatous cysts, the latter have come to assume a less subordinate position. The cavernous angiomas are far less concentrated to one locality in the brain, in contrast to the favored cerebellar habitat of the angiomatous cysts.

Forty-four cases of cavernous angioma have been found in the literature. The number reaches forty-nine, with the addition of the five cases included in this report. In nine of these cases (18 per cent), multiple tumors of the same character were scattered throughout the brain. In most of them, there were two or three angiomas (Finkelnburg, Jakob, Malamud, Müller and Ohlmacher), but in Creite's case there were eight, in Kufs' twelve, and in Huebschman's thirty; in Kalischer's case, the brain was studded with angiomas.

The distribution of these tumors is as follows: frontoparietal lobes, thirty-two; brain stem and fourth ventricle, fourteen; cerebellum, eight; in depth of cerebral hemisphere and third ventricle, nine; occipital lobe two.[2]

The gross appearance of a typical cavernous angioma is characteristic. It is spongelike and compressible because of the large spaces which one can usually see with the naked eye. It is always well circumscribed, but never encapsulated; its color is reddish brown because of the contained blood. Some of the tumors are soft, others firm, depending on the size of the blood spaces and the amount of connective tissue. Although they have a good venous and arterial blood supply, neither is excessive, and neither is disproportionate to the other. When opened at operation, they bleed freely and in proportion to the size of the cavernous spaces and the entering arterial supply. The bleeding is principally venous, though on the confines of the tumor the arterial bleeding may give some trouble. The tumors do not pulsate. The size of these tumors varies from minute areas to a mass larger than one's fist. The largest tumor in my series occurred in a baby, 1 month old. It was both intracranial and extracranial. Both portions were directly continuous through numerous small defects in the bone and dura.

Microscopically, these tumors show endothelial lined blood spaces with scant or not supporting coats, with a minimal amount of connective tissue between the blood spaces.

Thrombosis and calcification, principally the former, frequently occur, but apparently to a far less extent than in an arteriovenous aneurysm. Lindau has stained the tumors with glial stains to exclude the diagnosis of a glioma. Microscopic studies have been made exclusively

2. Where multiple tumors were present they have been entered in each location.

with hematoxylin and eosin stains, from which the diagnosis is easily made on the grosser aspects of the histologic picture.

Signs and Symptoms of Cavernous Angioma.—There is a striking uniformity in the symptoms when viewed as a whole. Occasionally, as in Kufs' patient who died at the age of 81, symptoms were not present. Other patients did not show symptoms until one of the vascular spaces suddenly ruptured and the patient died of a cerebral hemorrhage. Three patients from the group died in this way. This is a far smaller proportion of deaths from hemorrhage than in the group of arteriovenous aneurysms, probably owing to the arterial pressure in the defective walls of the latter.

A spontaneous cerebral hemorrhage occurring during the period of youth and middle age in a person without hypertension must nearly always indicate an underlying tumor or aneurysm. Most instances of so-called spontaneous "subarachnoid hemorrhage" arise in this way. At times the lesion is so small that it may be overlooked, or the vascular break may be a tumor of the spinal cord as in Lorenz's case. It is not fair to make a final anatomic diagnosis of primary "arachnoid hemorrhage" unless the spinal cord has been searched for angiomas, for these tumors are common throughout the central nervous system. Cases of angiomas of the spinal cord have been reported by Gaupp, Hadlick, Berenbruch, Lorenz, Roman, Pinner, Tannenberg, Lindau and Ritter. For the literature on this subject, the reader is referred to the publication of Tannenberg and Ritter.

The accompanying tables show at least three striking differences between cavernous angiomas and angiomatous cysts. 1. Most of the symptoms of cavernous angiomas are focal, and few are of general intracranial pressure. 2. The duration of symptoms is much longer. 3. The symptoms begin at an earlier age. Assuredly, these generalizations have their exceptions.

The clinical disturbances obviously depend on the location of the tumor as well as on its character. Tumors in the brain stem cause the most profound loss of function and affect life long before tumors in the silent lobes of the cerebral hemispheres. The symptoms in some of the cases of cavernous angioma occurring in early life are of short duration because the children so affected soon die.

In one of my patients, a tremendous cavernous angioma was present at birth. An external portion resembled an occipital meningocele; an internal portion pushed the cerebellum far forward and caused hydrocephalus. This tumor developed early in embryonic life, for at birth it was larger than one's fist. It doubtless developed early also because both the dura and occipital bone were honeycombed with parts of the tumor which connected the nerves within and without the skull. Kalischer's patient had convulsions soon after birth and died when he

was 1½ years old. In thirty patients, the age of onset of the symptoms could be computed. In eleven or about one-third, symptoms began before the tenth year; in eighteen, or 60 per cent, before the twentieth year, and in twenty-five, or 83 per cent, before the age of 30. (Only 16 per cent of the angiomatous cysts showed symptoms before the thirtieth year.)

The duration of the symptoms shows a contrast almost as striking. Six patients had symptoms for less than one year (three of these died of cerebral hemorrhage and one of operation); four had symptoms for two years; five for three years; and five, for from five to ten years; seven, for from ten to twenty years, and four, for from twenty to thirty years. In the group of patients with angiomatous cysts, 50 per cent had symptoms less than one year, whereas 80 per cent of those with cavernous angiomas had symptoms longer than one year, and 50 per cent had symptoms longer than five years.

By far the most common symptom of cavernous angioma is epilepsy, and usually the attacks are jacksonian. This is largely due to the fact that most of the tumors are in the cerebral hemispheres and near the rolandic area. It is highly improbable that a cavernous angioma located solely in the cerebellum will cause epilepsy. Many of the patients have had motor or sensory weakness, some slight, some transiently after an attack and others of severe grade.

Headache, vomiting and choked disk are infrequent in cerebral cavernous angiomas because the tumor rarely attains sufficient size to cause intracranial pressure. Rupture of a vessel in the tumor may at once induce intracranial pressure. One of my patients (case 24), with an angioma of the occipital lobe and a big cerebral hemorrhage, had a bilateral papilledema of high grade. Lewandowsky and Stadelmann reported a case presumably of angioma, in which a big cerebral hemorrhage was encountered by a puncture. The patient recovered.

Cavernous angiomas in the cerebellum and brain stem may cause hydrocephalus by closing the aqueduct of Sylvius or fourth ventricle, intracranial pressure then following. A high grade of hydrocephalus was present in all four of my cases of cerebellar cavernous angiomas. In one of these cases, the angioma was small and caused intermittent or recurring hydrocephalus, the tumor acting in ball-valve fashion. It is interesting that over a period of ten years the patient's attacks were intensified in three successive pregnancies. Finally, as the tumor grew, the ball-valve action was largely overcome, for her symptoms rarely abated. In another patient (case 20), slight trauma—presumably causing hemorrhage in the tumor, on several occasions, precipitated paralyses and general intracranial pressure. The first instance of this relationship occurred when the patient was 14 months old. The early age also indicates the probably congenital origin of the tumor. The relationship of

trauma and cerebral hemorrhage from vascular tumors was considered in the paper on arteriovenous aneurysms.

Two of my four cerebellar cavernous angiomas would easily have been tolerated in the cerebral hemispheres without symptoms of pressure. The other two were large. One had grown tightly into the brain stem. The changes in the reflexes in this group of tumors are usually of little help in making a diagnosis; the deep reflexes are increased along with motor disturbance; an ankle clonus and Babinski reflex are at times present, at other times absent. In midcerebellar tumors, bilateral reflex changes may be found.

TABLE 1.—*Analysis of Symptoms of*

Author	Date of Publication	Age	Sex	Type of Angioma: Cavernous	Type of Angioma: Small Solid Tumor with Cyst	Tumor: Single	Tumor: Multiple	Location of Tumor	Duration of Symptoms	Age at First Symptom	First Symptom	Signs and Symptoms of Intracranial Pressure	Focal Signs and Symptoms
Dandy.....	1928	44	M	Plexus	.....	+	..	Hypophyseal region.	6 years	38 years	Pains in eyes	Erosion of posterior clinoid process	Bitemporal hemianopsia and destruction of sella
Dandy.....	1928	2½	F	Plexus	.....	..	+	Sylvian fossa of each side	Since birth	Since birth	Large head	Yes, but not from angioma	.....
Dandy.....	1928	5 mo.	M	Plexus	.....	..	+	Sylvian fossa	1 mo.	4 mo.	Convulsions	None	Convulsions begin in face

X-ray examinations have not been helpful in my cases, for calcified lesions were not present in any of them; nor has any case from the literature been diagnosed from the roentgenograms. In one case, the convolutional atrophy of hydrocephalus was excellently demonstrated, but the large head and Macewen's sign (of separated sutures) had made the evidence given by the roentgenogram unnecessary.

Ventriculography was indispensable in making a diagnosis in two of my cerebellar cases, and ventricular estimation was useful in clinching the localization in another. These methods should always be used when the slightest doubt is entertained either of the existence of a tumor or of the location of a tumor that is known to exist.

Treatment of Cavernous Angioma.—Just as is true of angiomatous cysts, or for that matter any kind of tumor, the only satisfactory treat-

ment is extirpation, when this is possible. Some tumors lend themselves readily to removal; others present difficulties which are insuperable. One of my patients, a baby 1 month of age (case 21), died of shock when a bloody suboccipital angioma (the continuation of an intracranial tumor) was removed. Bleeding had to be controlled by plugging the big venous spaces in the bone with wax. A second patient, a boy, aged 16 (case 20), died one month after removal of a large cerebellar angioma which had grown into the brain stem. Death was not due to the tumor's removal which he survived, but to closure of the fourth ventricle caused by the formation of a cicatrix between the raw surfaces of the cerebellar

Cases of Plexiforme Angioma of the Brain

Epilepsy			Motor or Sensory Symptoms	Other Symptoms	Mentality	Operation	Cause of Death	Necropsy	Remarks	Studied Microscopically
Focal	Petit Mal	Grand Mal								
0	0	0	Pain in cheek and teeth	Diplopia	Normal	Tumor exposed, but inoperable	Operation	0	Patient was morphine addict; tumor was made up of coils of veins and resembled the well known venous plexus angiomas of the dorsal surface of the cord; the entire tumor could not be seen, nor could necropsy be obtained	0
0	+	0	Cannot sit up but uses both arms and legs	Failure to develop mentally and to coordinate muscular movements	Imbecile	+ Third ventriculostomy for hydrocephalus; angioma disclosed in sylvian fissure	Operation	+	Bilateral plexus of veins (angioma) in each sylvian fissure; several other small plexuses over both hemispheres; absence of corpus callosum; the angiomas did not cause the mental or physical disturbances, they were merely incidental conditions; stricture at iter caused hydrocephalus	0
+	+	+	None	None	Infant	Exploration	Operation	+	Two typical venous plexuses about 2 cm. apart; they were connected by communicating branches and emptied into the sylvian vein	+

lobes and pons from which the tumor had been removed. In this case, the foramina of Luschka had long been sealed by the tumor.

A third patient died before operation. This should have been much the easiest tumor of the group to have extirpated, had it been found at operation. There was a huge blood-filled cavity in the parieto-occipital lobes. The walls of the cavity were rough, having been carved out of the white matter of the brain which hung in shreds in the cavity; in this respect, it was entirely unlike the smooth cyst associated with an intracystic angioma.

Two of the cavernous angiomas were entirely removed, and the patients are apparently well. In one patient (case 22), the tumor was excised from the left lobe of the cerebellum with a margin of cerebellar tissue. It is now over two years since the operation. She is entirely well and without residual cerebellar symptoms.

TABLE 2.—*Analysis of Symptoms in Cases*

Author	Date of Publication	Age	Sex	Type of Angioma: Cavernous	Type of Angioma: Small Solid Tumor with Cyst	Tumor: Single	Tumor: Multiple	Location of Tumor	Duration of Symptoms	Age at First Symptom	First Symptom	Signs and Symptoms of Intracranial Pressure	Focal Signs and Symptoms
Baum.....	1911	21	M	..	+ cyst contained yellow fluid	..	..	Left parietal	.....	.....	Convulsions and coma	Coma	Jacksonian attacks
Bielschowsky..	1902	24	F	..	+ small solid tumor in large cyst	+	..	Right frontal lobe	14 mo.	23 yr.	Headache and dizziness	Choked disk, vomiting, headache	Facial weakness, positive Romberg, increased reflexes
Bruns.....	1897	24	M	..	+	..	..	Left parietal	.....	.....	Convulsions	No	Jacksonian attacks
Friedrich and Stiehler	1922	41	M	..	+	..	+	Cerebellum	2 yr.	39 yr.	Pain in neck	Headache, vomiting, loss of vision	.....
Koch.....	1913	47	M	+ one side	+ other side	..	+	Each cerebellar lobe	3 yr.	44 yr.	Glycosuria	+	.....
Lindau.....	1926	26	F	..	+	+	..	Cerebellum	5 yr.	21 yr.	Headache	Headache; vomiting, choked disk	Staggering, ataxia, nystagmus, loss of corneal reflex
Lindau.....	1926	50	M	..	+	+	..	Cerebellum	6 mo.	49 yr.	Headache	Headache, vomiting; choked disk	Staggering gait and Romberg, nystagmus
Lindau.....	1926	42	F	..	+	+	..	Cerebellum	4 yr.	38 yr.	Headache	.....	.....
Lindau.....	1926	37	M	..	+	..	..	Cerebellum	8 yr.	29 yr.	Headache	Headache, vomiting, choked disk	Staggering to right, nystagmus
Lindau.....	1926	28	F	..	+	+	..	Cerebellum	1 yr.	27 yr.	Headche and stiff neck	Headache, vomiting	None
Lindau.....	1926	46	M	..	+	+	..	Cerebellum	6 mo.	45 yr.	Headache	Headache, choked disk	Romberg, falls to right
Lindau.....	1926	40	F	..	+	+	..	Cerebellum	1 yr.	39 yr.	Dizziness and staggering	Headache, lumbar puncture	Romberg and staggering
Lindau.....	1926	33	F	..	+	+	..	Cerebellum	2 yr.	31 yr.	Weakness	Headache, vomiting, choked disk	.....
Lindau.....	1926	..	..	..	+	+	..	Cerebellum	.....	.....	.....	.....	.....
Lindau.....	1926	52	M	..	+	+	..	Cerebellum	.....	.....	.....	.....	Loss of left facial and trigeminal functions
Lindau...	1926	33	M	..	+	+	..	Cerebellum	. ....	.....	.....	Choked disk	.....
Lindau..... ...	1923	32	M	..	+	+	+	Cerebellum and medulla	.....	.....	.....	.....	.....
Lindau.....	1926	38	F	..	+	+	..	Cerebellum	.....	.....	Headache	Choked disk	.....
Luzzatto.....	1925	..	..	..	+	+	..	Medulla	.....	.....	.....	.....	Paresis left face, disturbance of speech and gait

Epilepsy			Motor or Sensory Symptoms	Other Symptoms	Mentality	Operation	Cause of Death	Necropsy	Remarks	Studied Microscopically
Focal	Petit Mal	Grand Mal								
+	..	+	.....	No	Good	+ with finger extirpation	.....	+	Patient in coma when operated on; no previous symptoms; solid tumor size of walnut; died one year later of pneumonia	+
0	..	0	Dizziness; diplopia	.....	.....	0	Intracranial pressure	+	Large cyst with hazelnut sized solid tumor; cerebellar tumor suspected	+
+	..	+	Weakness in right leg also paresthesia	.....	.....	+	Meningitis, postoperative	+	.....	+
..	..	..	.....	.....	.....	0	Intracranial pressure	+	Small angioma in cerebellum, another in pons and one in medulla	+
..	..	..	.....	Diabetes	Normal	0	.....	+	Patient had von Hippel's disease; cysts of pancreas (with diabetes); cysts and angiomas of liver	+
0	..	0	Left facial paralysis	.....	Normal	0	Intracranial pressure	..	Cyst with angioma—hydrocephalus; cysts of pancreas, cysts of kidneys; hypernephroma	+
0	..	0	Weakness left arm and leg; trigeminal pain	Babinski + loss of corneal reflex	Normal	Decompression	Intracranial pressure	+	Cyst 3 by 2 by 1.5 cm.; tumor 1 by 2 by 1 cm. in upper part of cyst; hydrocephalus	+
0	..	0	.....	.....	.....	0	Intracranial pressure	+	Cyst 5 by 6 by 2 cm.; smooth wall; tumor 1 by 1 cm.	+
0	..	0	.....	Loss of corneal reflex	.....	0	Died 24 hours after spinal injection of air	+	Cyst 6 by 4 by 2 cm.; tumor 1.5 by 1.5 by 0.7 cm.; adenoma of both suprarenal glands; hydrocephalus	+
0	..	0	.....	Both corneal reflexes diminished	.....	0	Intracranial pressure	+	Cyst 3 by 2 by 2 cm.; tumor 1 by 1 cm.	+
+	+	+	.....	Rigid neck	.....	0	Intracranial pressure	+	Cyst 4 by 5 by 2 cm.; tumor 1 by 0.5 cm.; hydrocephalus	+
..	..	..	.....	Adiadokokinesia	.....	0	Intracranial pressure	+	Cyst with angioma; hydrocephalus	+
..	..	..	Weakness both legs	Blindness	... .	0	Tonic convulsions	+	Small angioma in cyst.....	+
..	..	..	.....	.....	.....	.....	.....	+	Museum preparation	+
..	..	..	... .	Nystagmus blindness	.....	Trephine	Intracranial pressure	+	Cyst 4 by 4 by 1.5 cm.; tumor 1 by 0.5 cm.	+
..	..	..	.....	.....	.....	.....	Intracranial pressure	+	Cyst with angioma in the wall	+
..	..	..	.....	.....	.....	.....	Intracranial pressure	+	Large cyst with angioma; also several small angiomas in cerebellar lobes (largest size of pea) one in medulla	+
..	..	..	.....	Tremor of fingers of both hands	.....	.....	Intracranial pressure	+	.....	+
0	..	0	Weakness of left face	.....	Suggestive of a neurosis	0	.....	+	Patient had a cavernoma of medulla with cyst formation like a syringomyelia	+

The other successful extirpation was a tumor laying on the pons and medulla (case 23). During the dissection, the tumor was thought to be a "venous aneurysm," because there seemed to be a single sac with several large venous outlets and because it was so compressible. After

TABLE 2.—*Analysis of Symptoms in Cases—*

Author	Date of Publication	Age	Sex	Type of Angioma: Cavernous	Type of Angioma: Small Solid, Tumor with Cyst	Tumor: Single	Tumor: Multiple	Location of Tumor	Duration of Symptoms	Age at First Symptom	First Symptom	Signs and Symptoms of Intracranial Pressure	Focal Signs and Symptoms
Newmark.....	....	32	F	..	+	+	..	Cerebellum	1½ yr.	30 yr.	Pain in back of head	Headache, vomiting, diplopia, choked disk	Occipital pain, buzzing left ear
Schlaffer.....	1926	40	M	..	+	+	..	Cerebellum	9 mo.	39 yr.	Headache	Headache, choked disk	Staggering gait, falls backward to left
Schweyer.....	1914	23	M	+	+	+	..	Frontoparietal lobe	13 yr.	12 yr.	Convulsions	No	Jacksonian attacks
Dandy.....	1928	32	F	..	+	+	..	Vermis of cerebellum	7 mo.	31 yr.	Headache	Headache, vomiting, choked disk with tremendous retinal hemorrhages	Staggering gait and positive Romberg
Dandy.....	1928	33	F	..	+	+	..	Cerebellum	6 mo.	35 yr.	Headache	Headache, vomiting, choked disk	Staggering gait, Romberg, ataxia, nystagmus, adiadokokinesia
Dandy.....	1928	44	F	..	+	+	..	Cerebellum vermis	2 mo.	44 yr.	Dizziness and headache	Headache, vomiting, choked disk	Staggering gait, ataxia
Dandy.....	1928	28	M	..	+	+	..	Cerebellum, left lobe	6 mo.	27 yr.	Headache (in attacks)	Coma, choked disk	Staggering gait
Dandy.....	1928	35	M	..	+	+	..	Cerebellum, left lobe	3 mo.	35 yr.	Occipital headache	Headache, vomiting, choked disk	Staggering gait, Romberg, ataxia
Dandy.....	1928	34	M	..	+	+	..	Vermis of cerebellum	2 yr.	32 yr.	Pain in eyes and occiput	Headache, vomiting, choked disk	None
Dandy.....	1928	40	M	..	+	..	..	Left cerebellar lobe	1 yr.	39 yr.	.....	Headache, vomiting, choked disk	Staggering gait

removal and section of the tumor, it was seen to be a typical solid cavernous angioma. The mass was dissected with great care after ligating the large venous outlets as shown in the accompanying drawings (figs. 27, 28, 29 and 30). No artery of size was seen to enter the tumor. There was no injury to the brain stem or cerebellum during the dissection. The patient also is well, one year after operation.

REPORT OF CASES OF CAVERNOUS ANGIOMA

CASE 20.—*Cavernous Angioma of the Cerebellum and Brain Stem.*

The patient was a very well nourished boy, aged 16, with a large head. He had been bedfast for sometime and sought relief for headache, disturbance of

Cyst with Angioma in the Wall—Continued

Epilepsy			Motor or Sensory Symptoms	Other Symptoms	Mentality	Operation	Cause of Death	Necropsy	Remarks	Studied Microscopically
Focal	Petit Mal	Grand Mal								
0	+	0	.....	Attacks of moment's loss of consciousness	Normal	0	Intracranial pressure	+	Pea sized tumor in extracerebellar; collection of yellow fluid (left cerebellar lobe)	+
..	..	..	Bilateral Babinski	Dizziness	.....	Extirpation with lobe of cerebellum	Living	..	Large part of cerebellum removed with tumor	+
+	..	+	None	None	Normal	0	Status epilepticus	+	Cyst size of cherry, filled with blood; tumor size of small walnut alongside; some calcification	+
0	0	0	Occasional attacks of numbness of right arm and leg	Stiff neck dizzy attacks	Normal	Removal	Living and well, 5 years	..	In a large cyst filling the vermis was a small papilloma (angioma); it lay over the midbrain; totally removed; vision has returned to normal	+
Tonic spasms of whole body; no loss of consciousness			Transient ankle clonus on right	Dizziness; stiffness of neck; diplopia	Normal	Removal of angioma in the wall	Living, 2 mo.	..	A half pea-sized angioma was located in the tonsil of cerebellum	+
Tonic spasms but no loss of consciousness			Positive Babinski	Dizziness	Mental cloudiness	.....	Intracranial pressure	+	Cyst in vermis of cerebellum tiny plaque of angioma over region of the midbrain	+
0	0	0	Reflexes normal	Dizziness diplopia	Normal	Removal of angioma	Living; 7 years since operation	..	Localization of tumor by ventriculography	+
0	0	0	Reflexes normal	Blind; dizziness; stiff neck	Normal	Removal of angioma	Living; 4 years	..	Ventricular estimation test substantiated cerebellar localization	+
0	0	0	Numbness and tingling in right arm and leg	.....	Normal	Removal of angioma	Living; 6 months	..	Localization of tumor made solely by ventriculography	+
..	..	..	.....	.....	Normal	.....	Intracranial pressure	+	Patient died before reaching hospital	+

vision, disturbance of gait and projectile vomiting. His symptoms dated back to the age of 14 months, when he had fallen a distance of 4 feet, striking the back of the head on a brick. He had been unconscious for only a few minutes, but immediately afterward had become paralyzed on both sides. The father, who is a physician, insisted that both sides were paralyzed at that time. After three weeks, the paralysis had gradually cleared up; both sides had improved about the same time. The father said further that the child had been talking for about

TABLE 3.—*Cases of Multiple Cavernous*

Author	Date of Publication	Age	Sex	Type of Angioma: Cavernous	Type of Angioma: Small Solid Tumor with Cyst	Tumor: Single	Tumor: Multiple	Location of Tumor	Duration of Symptoms	Age at First Symptom	First Symptom	Signs and Symptoms of Intracranial Pressure	Focal Signs and Symptoms
Creite.....	1903	21	F	+	..	..	+	See under remarks	19 yr.	2 yr.	Convulsions	No	No
Finkelnburg...	1905	14	M	+	..	..	+ two	See under remarks	2½ yr.	11 yr.	.....	Choked disk	Staggering gait, left abducens palsy
Huebschmann.	1921	39	M	+	..	..	+ about 30 in all	Scattered	.....	.....	Convulsions	.....	.....
Jakob.....	1924	34	F	+	..	..	+	See under remarks	20 yr.	10 yr.	Convulsions	Pains in head	Weakness left side; jacksonian attacks
Kalischer.....	1897	1½	..	+	..	..	+	See under remarks	1 yr.	6 mo.	Convulsions	No	Jacksonian attacks and later paralysis
Kufs.....	1928	81	M	+	..	..	+	Both hemispheres pons	No symptoms	.....	None	None	None
Malamud.....	1925	51	F	+	..	..	+	See remarks	22 yr.	39 yr.	Headache	Diplopia, headache, dizziness	Symptoms like paralysis agitans 3 years before death
Müller.....	1923	17	M	+	..	..	+	Caudate nuclei (both sides)	5 days	17 yr.	Headache	Pain in head, coma, bradycardia	.....
Ohlmacher.....	1899	..	..	..	..	..	+	See under remarks	.....	.....	.....	.....	.....
													Cases of Cavernous Angioma in
Astwazaturow	1911	35	F	+	..	+	..	Right fronto-parietal	2 yr.	33 yr.	Headache	+	Attacks in face, arm and legs
Astwazaturow	1911	23	F	+	..	+	..	Right temporal lobe	13 yr.	10 yr.	Convulsions	No	Jacksonian epilepsy
Bail.....	....	10	M	+	..	+	..	Left rolandic area	2 yr.	8 yr.	Convulsions	+ choked disk	Jacksonian epilepsy
Bremer, d'Antona	Ref. Lechner	20	M	+	..	+	..	Parietal	.....	.....	Convulsions	.....	Jacksonian attacks beginning in thumb
Bremer and Carson	Ref. Lechner	23	..	..	..	..	..	Subcortical	.....	.....	.....	.....	.....
Cassirer and Muhsam	1911	22	M	+	..	+	..	Right parietal postcentral	5 yr.	17 yr.	Convulsions	Headaches since youth	Jacksonian attacks sensory type, beginning in left hand

Epilepsy			Motor or Sensory Symptoms	Other Symptoms	Mentality	Operation	Cause of Death	Necropsy	Remarks
Focal	Petit Mal	Grand Mal							
0	..	+	No	.....	.....	0	Convulsions	+	Eight isolated tu same small struc scattered throug bral hemispheres in the cerebellum the pons; vessels cified
0	..	0	.....	Diplopia, difficulty in urination, pains in back and limbs	.....	0	Pressure	+	Small tumor in ce rigemina; large fourth ventricle into spinal c causes hydrocep
..	..	+	.....	.....	.....	0	Convulsions	+	About thirty tin were scattered brain
+	..	+	Weakness left side	Intention tremor, ataxia, dysarthria	.....	0	Convulsions	+	Three tumors were small: (1) in (2) in pons, (3 ventricle
+	..	+	Weakness right side	.....	.....	0	Convulsions	+	Left hemisphere small tumors faces; hemipleg developed
0	..	0	None	.....	Senile dementia	0	Senility	+	Nevi in skin pr lated; daughter (recovery) at ag small tumors throughout whi brain, one in po another in po cavernomas in
0	..	0	.....	Extraocular palsies, queer feeling in both hands	Attacks of euphoria, depression and apathy	0	.....	+	Tumors (1) in reg dibulum and th (1.5 by 2.75 cm.) pallidum (3 by 5 pons, and medu others scattered isphere
..	..	..	.....	Extraocular palsies, cervical rigidity	.....	.....	Hemorrhage	+	Small tumor in ea of each side; pa days after first hemorrhage
..	..	..	.....	.....	.....	0	.....	+	Three angiomas v all small; (1) ce (2) optic thalam cord; an oste fibroendothelion present
Fronto-Parietal Region of the Brain									
+	..	+	.....	Loss of memory	Retrograde amnesia	0	Meningitis	+	Tumor size of "n thrombosed an
+	..	+	.....	Loss of memory	Loss of memory	0	Convulsions	+	Tumor extends hippocampus
+	..	+	.....	.....	.....	0	Convulsions	Large tortuous mass of veins on surface	Attacks followed after slight hea sibly an arteri rysm
+	..	+	.....	.....	.....	+	.....	..	.....
..	..	+	.....	.....	.....	+	.....	..	Tumor size of a
+	+	+	Loss of touch eventually	Weakness of hand after attacks	Slow at school	+ removed	Living	..	Patient complain ache after exer culty with hem tumor excised

TABLE 3.—*Cases of Multiple Cavernous Angioma*

Author	Date of Publication	Age	Sex	Type of Angioma: Cavernous	Type of Angioma: Small Solid Tumor with Cyst	Tumor: Single	Tumor: Multiple	Location of Tumor	Duration of Symptoms	Age at First Symptom	First Symptom	Signs and Symptoms of Intracranial Pressure	Focal Signs and Symptoms
Worster-Drought and Dickson	1928	31	M	+	..	+	..	Fronto-parietal	3 yr.	27 yr.	Convulsions	Severe head pains coma	Jacksonian attacks in left side of face
Engelhardt....	1904	26	M	+	..	+	..	Right parietal 4×3×3 cm.	23 yr.	3 yr.	Convulsions	No	Jacksonian attacks
Krause.....	1911	18	M	+	..	+	..	Left parietal	17 yr.	1 yr.	Convulsions	No	Paralysis of right arm after attacks when 1 year old
Krause.....	1911	10	M	+	..	+	..	Left parietal	1 yr.	9 yr.	Convulsions	Choked disk	+
Leischner.....	1909	39	M	..	..	+	..	Left parietal	10 yr.	29 yr.	Convulsions	Headaches	Attacks begin in right side of face
Lewandowsky and Selberg	1913	45	F	+	..	+	..	Right frontal	.....	.....	Convulsions	No	Jacksonian attacks
Luschka.....	1854	40	M	+	..	+	..	Left frontal	.....	.....	.....	.....	.....
Peán.....	....	15	M	+	..	+	..	Parietal lobe	.....	.....	Convulsions	.....	Jacksonian attacks
Poirier.....	....	34	M	+	..	+	..	Right parietal lobe	3 yr.	.....	Headaches	Headaches	Jacksonian attacks
Powers.....	1913	45	F	+	..	+	..	Right frontal	6 mo.	44 yr.	Convulsions	None	Head to left in convulsions
Starr and McCosh	1894	21	M	+	..	+	..	Left frontal	16 yr.	5 yr.	Pain in head	Pain and headache	Pain left side of head
Strominger....	1903	Infant	..	Mass of vessels in meninges	..	+	..	Meninges left side	Infancy	.....	.....	.....	.....
Struppler.....	1904	48	F	+	..	+	..	Left rolandic area	Few weeks	48 yr.	Convulsions	None	Attacks in right foot
Volland.....	1913	..	..	+	..	+	..	Falx surface of right hemisphere	.....	.....	.....	.....	.....
Cases of Cavernous Angioma in													
Herman.....	1923	40	F	+	..	+	..	Right occipital lobe	10 yr.	30 yr.	Coma	None	Jacksonian attacks
Dandy.....	1928	34	M	+	..	+	..	Right occipital lobe	2 yr.	31 yr.	Pain in leg, and vertigo	Headache, choked disk	None
Cases of Cavernous Angioma Situated Deeply in													
Stief.....	1924	22	M	+	..	+	..	Third ventricle	.....	.....	.....	.....	Disturbance of gait and speech
Uyematsu.....	1920	..	..	+	..	+	..	Corpus callosum	.....	.....	.....	.....	.....

of the Brain from the Literature—Continued

Epilepsy			Motor or Sensory Symptoms	Other Symptoms	Mentality	Operation	Cause of Death	Necropsy	Remarks	Studied Microscopically
Focal	Petit Mal	Grand Mal								
+	..	+	Hemiplegia	Sudden hemiplegia	.....	0	Intracranial pressure	+	Coma followed ten days after hemiplegia	+
+	..	+	.....	.....	.....	0	Convulsions	..	First convulsions at age of three years; then no more until sixteen years old; steadily increasing; tumor largely calcified	+
+	..	+	Weakness right side	.....	.....	Removal	+	No	.....	+
+	..	+	Weakness right side after attacks	.....	.....	Removal	+	No	.....	+
+	..	+	Right side weak after attacks	Dizziness aphasia	.....	Removal	+	No	Paralysis after early attack; function largely returned but weakness increased after attacks	+
+	..	+	.....	Suggestive left Babinski	.....	Removal	+	No	.....	+
..	..	..	.....	.....	.....	0	.....	+	.....	+
+	..	+	.....	.....	.....	+	.....	..	.....	+
+	..	+	Weakness of left side	.....	.....	+	.....	..	.....	+
0	..	+	None	None	.....	0	Convulsions	+	Angioma is sharply outlined in brain; walls of blood spaces are made up of connective tissue and not neuralgia	+
0	0	0	.....	.....	Excitable; often violent; not balanced	Removal	+	No	Patient unconscious twelve hours after a blow at age of 5; pain in left side of head since; another period of unconsciousness after blow at age of 16; eager to study but excitable; gives way easily to emotions; fairly bright	+
..	..	..	Hemiplegia	.....	.....	0	.....	+	Angioma of meninges—pushed brain away; patient had nevus on face	+
+	..	+	.....	.....	.....	0	Convulsions	+	Tumor size of hazelnut; no convulsions until age of 48; then seventy-five in twelve hours	+
..	..	..	.....	.....	.....	0	.....	+	Tumor size of hickory nut....	+
Occipital Region of the Brain										
+	..	+	.....	.....	.....	0	Convulsions	+	At age of 30 patient had first convulsion; no more until ten years later when she had three more; died in status epilepticus	+
0	0	0	Pain in arms and legs	Stiff neck, vertigo, diplopia	Normal	0	Hemorrhage from tumor	+	Patient died the day before the time set for operation; a large hemorrhage had resulted from a small cavernous angioma in the occipital lobe	+
the Brain and in the Region of the Third Ventricle										
0	..	0	.....	.....	Normal	0	.....	+	Tumor size of walnut grew upward from region of infundibulum into both hemispheres to corpus callosum and projected into both lateral ventricles	+
..	..	..	.....	.....	.....	0	.....	+	.....	+

TABLE 3.—*Cases of Multiple Cavernous Angioma*

Cases of Cavernous

Author	Date of Publication	Age	Sex	Type of Angioma: Cavernous	Type of Angioma: Small Solid, Tumor with Cyst	Tumor: Single	Tumor: Multiple	Location of Tumor	Duration of Symptoms	Age at First Symptom	First Symptom	Signs and Symptoms of Intracranial Pressure	Focal Signs and Symptoms
Levick.....	1914	9	F	+	..	+	..	Cerebellum	Rapid progression	.....	Paralysis	Headache	Cerebellar symptoms
Lindau.....	1926	48	M	+	..	+	..	Cerebellum	6 yr.	42 yr.	Headache	Vomiting, headache, choked disk	.....
Lindau.....	1926	..	..	+	..	..	+	Cerebellum and pons	.....	.....	.....	.....	.....
Dandy.....	1928	16	M	+	..	+	..	Vermis of cerebellum	15 yr.	1 yr.	Paralysis bilateral after slight trauma	Large head, choked disk, convolutional atrophy of skull, headache, vomiting	Hydrocephalus; staggering gait; Romberg
Dandy.....	1928	1 mo.	M	+	..	+	..	Suboccipital intra and extracranial	Before birth	Tumor was present at birth	Tumor	Hydrocephalus with large head	Tumor resembles meningocele
Dandy.....	1928	35	F	+	..	+	..	Left cerebellar lobe	10 yr.	25 yr.	Headache	Headache, choked disk	Partial deafness on left

Cases of Cavernous Angioma in

Berblinger.....	1922	27	M	+	..	+	..	Medulla	13 yr.	14 yr.	Paralysis	+	Paralysis first one arm, then other
Enders.....	1908	60	M	+	..	+	..	Left side of pons	.....	.....	Convulsions	No	Attacks begin in right side of body
Leyser.....	1922	20	F	+	..	+	..	Pons 1 by 3 mm.	20 days	20 yr.	Coma	Coma	.....
Nalin.....	1928	11	M	+	..	+	..	Fourth ventricle	9 mo.	10 yr.	Headache	Coma (no choked disk)	Staggering gait, nystagmus, ataxia, adiadokokinesis
Nambu.....	1907	63	..	+	..	+	..	Pons	.....	.....	.....	.....	.....
Schuback.....	1927	28	F	+	..	..	+	Fourth ventricle	5 yr.	23 yr.	Headaches	Headache, loss of vision	Staggering gait, nystagmus, ankle clonus and Babinski
Tophoff.....	1925	28	F	+	..	+	..	Pons	.....	.....	.....	.....	.....
Wohlwill.....	1927	28	F	+ with von Hippel's	..	..	+	Fourth ventricle spinal cord	5 yr.	23 yr.	+	+	Weakness left leg
Dandy.....	1928	31	M	+	..	+	..	On pons and medulla	2½ yr.	29 yr.	Stiffness of right leg in spells	Headache, choked disk, dimness of vision	None, diagnosis by ventriculography

of the Brain from the Literature—Continued

Angioma in Cerebellum

Epilepsy			Motor or Sensory Symptoms	Other Symptoms	Mentality	Operation	Cause of Death	Necropsy	Remarks	Studied Microscopically
Focal	Petit Mal	Grand Mal								
0	..	0	Weakness of left leg and face	Occipital pain, reflexes increased on left	.....	Removal +	.....	No	....	+
..	..	..	.....	.....	.....	.....	Intracranial pressure	+	Large solid angioma in cerebellar lobe, mostly capillary spaces, others larger	+
..	..	..	.....	.....	.....	.....	.....	+	Three angiomas, one in pons and two in cerebellum; all very small—museum specimen	+
0	0	0	Bilateral at times	Strabismus	Normal	+ Removal of tumor	Hydrocephalus	+	This angioma had grown into the medulla and pons; on several occasions slight trauma induced signs and symptoms suggestive of hemorrhage into the tumor	+
0	0	0	None	None	Baby	Removal of extracranial tumor	Shock	+	Very large tumor outside the skull and another even larger inside and directly beneath; both were continuous by extension of tumor directly through occipital bone	+
0	0	0	Numbness of left side after spell of headache	Anosmia	Normal	Removal	Living and well	..	Tumor was removed with zone of normal cerebellar tissue; complete recovery; localization made by ventriculography	+
Brain Stem and Fourth Ventricle										
0	..	0	Paralysis	Urinary incontinence	Normal	0	.....	..	Associated with von Hippel's disease	+
?	..	+	No	.....	.....	0	Convulsions	+	Tiny tumor in pons, more to left side	+
0	..	0	Paralysis	.....	.....	0	Hemorrhage (?)	+	.....	+
0	..	0	.....	.....	.....	0	Intracranial pressure	+	Tumor filled fourth ventricle, pushed into pons; hydrocephalus	+
..	..	..	.....	.....	.....	.....	.....	+	Small tumor	+
0	..	0	Left-sided paralysis	Difficulty in urination	.....	0	Intracranial pressure	+	(1) tumor size of walnut in fourth ventricle; (2) another in dorsal spinal cord; (3) retinal angioma (von Hippel's disease); (4) cysts of pancreas and kidney	+
..	..	..	.....	.....	.....	0	Apoplexy	+	Patient died of apoplexy.....	+
+	..	+	Weakness left side of body	.....	.....	0	Intracranial pressure	+	Tumor size of hazelnut in roof of fourth ventricle; another tumor (2 cm.) in dorsal cord; von Hippel's tumor of retina; cysts of pancreas and kidney	+
0	0	0	Numbness and weakness of left side, increased at times	Loss of vision, uncertain gait, but not staggering	Normal	Removal	Living and well	..	Tumor completely removed (by dissection) from floor of fourth ventricle	+

three months prior to the injury, and that after the blow on the head speech had been lost but had returned with the motor function. His head had always been large, but the father explained that this was a family characteristic; all of the father's brothers had large heads. The boy, however, wore a 7¾ hat, while the size of his father's hat was 7½; his grandfather wore a No. 8. During the convalescence from the injury to the head, the patient had vomited a great deal and had cried much after the initial drowsy period wore off. Even after six weeks, the vomiting and crying had persisted. The patient had continued to have headaches and spells of vomiting up to the age of 6 years; at this time he had been thrown from a horse and had been unconscious for about half an hour. During the next two days, he had been unable to stand. He had always been more clumsy than the other children, and his movements were slower and less sure. After the age of 6, the clumsiness had increased. When he was 2½ years old, it had been noticed that a crossed eye had developed without warning; the right eye drew in toward the nose. For sometime after the injury to the head (at the age of 6), the eyeball had not moved; this condition had improved gradually during the next six months, some weakness of the external rectus muscle persisting. Until the age of 12, there had been little change in his condition. He could not read well because of the extra-ocular palsies; his clumsiness seemed to increase, and he became weaker and had a tendency to deviate to the right side while walking.

At the age of 12, he had tripped and fallen on the right side of the head while running at school. He had been unconscious for twenty minutes and drowsy for several days; during this time he had had a fever and his temperature had been as high as 103 F.; he had complained of a severe headache. Again he had been unable to walk for a period of sixty-one days, and during all of this time he had complained of severe headaches. After two months he had begun to walk, but only with support. Two weeks later, he had been able to stand alone. For the following two years, nothing unusual had happened, and then without warning the headaches had reappeared and had occurred more or less constantly; they were always severe and occurred every two or three weeks.

A year before operation, the boy's father had noticed that his disturbance of gait, awkwardness and clumsiness were still persisting. At this time, it had been noticed that he staggered definitely toward the right. Two months before operation, the patient had become progressively worse, and during all of this time he had been confined to bed.

Examination showed a rather sallow, fat boy with a large bony frame and poor musculature. He complained of severe headache. His large head was disproportionate to the development of his body, and showed a marked cracked pot sound on tapping along the frontoparietal sutures. The veins of the eyelids and scalp were prominent and full. The eyegrounds showed a slight choking of both disks, perhaps a little more marked on the right; the temporal margins, however, were still visible. Weakness of both external rectus muscles produced an evident strabismus. There was slight but definite weakness of the right facial muscles. His hearing was impaired on both sides, but air conduction was better than bone conduction. The entire right side of the body was definitely weaker than the left. There was a marked positive Romberg sign, and he always fell to the right. Ataxia was present in both hands, but more on the right. There was adiodokokinesis on both sides, more on the right, and nystagmus in both directions. Reflexes were equal and active. The Babinski sign was absent. X-ray examination showed separation of the suture.

It was evident that the patient had a cerebellar lesion and presumably a tumor. It was also evident that this lesion had been present since the age of 14 months, so that it must have been congenital. As the symptoms of localization and those of general pressure increased after slight trauma, it seemed probable that the lesion must have been a tumor which was readily susceptible to hemorrhage. The diagnosis of a cerebellar tumor was made.

Operation.—On June 19, 1925, a bilateral cerebellar exposure was made. The lesion was at once evident in the vermis and the mesial side of both cerebellar lobes; it presented a brownish discoloration and was extremely hard and inelastic. Although sharply circumscribed, it was not encapsulated. In order to gain a better impression of the lesion, the foramen of Magendie and the fourth ventricle were exposed. The cerebellar lobes were separated in order to reach the tumor in the fourth ventricle. After proceeding about 2 cm. along the floor of the fourth ventricle, several large veins were encountered running directly out of the brain stem into the hard indurated mass of tumor, which was continuous with the mass described on the surface. The entire fourth ventricle was obliterated at its level

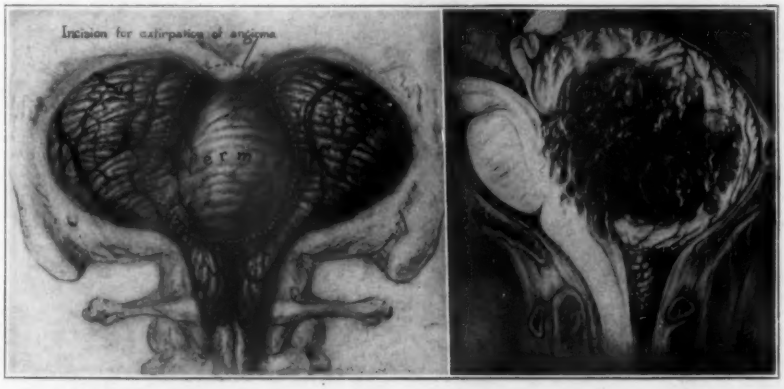

Fig. 20 (case 20).—Drawing to show position and character of the cavernous angioma. The gross character of this tumor borders on that of a plexiforme angioma. The dotted line indicates the line of incision for resection of the tumor laterally. Since there was no plane of cleavage between the tumor and the brain stem, the tumor was sectioned directly above the medulla and pons, leaving a fragment of the angioma attached thereto. Many of the vessels were thrombosed and as all of the bleeding was venous the excision of the tumor was not accompanied by much hemorrhage despite its vascular construction. The tumor had completely closed the fourth ventricle and produced hydrocephalus.

by the tumor, which did not give any outward evidence of being more than dense fibrous tissue. As large veins were present everywhere and were coming directly out of the medulla, extirpation seemed hopeless. The wound was closed.

The patient's condition remained practically unchanged for the next ten days. After further thought and in view of the hopeless nature of the lesion, I was persuaded to make an attempt to remove the tumor, though it was clear that it would be necessary to carve the tumor from the brain stem, into which it had grown.

Second Operation.—On June 30, 1925, the cerebellar wound was reopened. The entire vermis and the inner margin of each cerebellar lobe was then prepared for

resection with the tumor. Preparatory to this section, the veins on the surface were ligated, and the large veins which ran from the surface of the cerebellum to the tentorium were doubly ligated and divided. The incision was then carried through the cerebellar cortex beyond the confines of the tumor (fig. 20). Much to my surprise, no vessels of moment were encountered during this part of the dissection. The hemispheres were retracted to either side. The tumor then remained attached only to the floor of the fourth ventricle, i. e., the pons and medulla.

The anterior surface of the mass was found to be well defined and ended just posterior to the aqueduct of Sylvius. The portion of the fourth ventricle between the aqueduct and the obstruction was greatly dilated, and the aqueduct was as large as one's little finger. The release of this fluid greatly facilitated the operation. The dissection was then begun along the floor of the fourth ventricle. There was no line of cleavage; the mass of fibrous tissue was densely adherent to the brain stem, and from this source the large veins were seen to enter, as at the previous operation. There seemed to be no alternative than to deliberately cut through

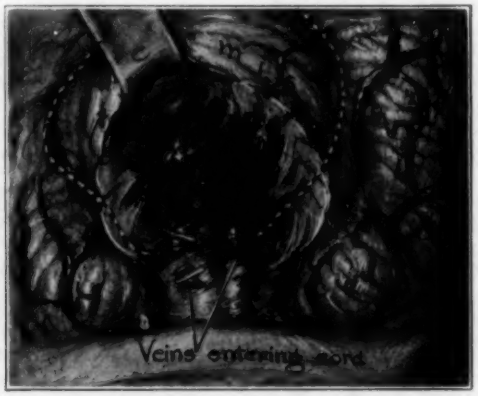

Fig. 21 (case 20).—Operative attack on the tumor over the medulla and pons. This was the only difficult part of the extirpation.

the mass just above the floor of the ventricle, and to control the bleeding with silver clips and with packs. It now seemed fairly certain that the lesion was not an arteriovenous aneurysm and that the struggle with hemorrhages would be mainly with veins. Much to my surprise, however, these enormous veins bled relatively little, and many of them were thrombosed; it was possible to cut through the entire scar with little bleeding, and this was readily controlled (fig. 21). The mass of tumor was then lifted out of its bed. The wound was closed without drainage.

Recovery from the immediate effects of the operation was uneventful. The patient did not have any immediate effects from the removal of the tumor mass. He lived one month after the operation. About ten days after the operation, it was evident that the hydrocephalus still persisted, for there was steadily increasing pressure on the cerebellar wound.

Necropsy showed that the three sides of the raw surface produced by the extirpation of the tumor had closed together and had again completely closed the fourth ventricle. All of the vascular fibrous mass had been removed, except the portion which was deliberately left on the floor of the ventricle.

The microscopic diagnosis was cavernous angioma. It doubtless was of congenital origin.

CASE 21.—*Cavernous Angioma in Posterior Cranial Fossa and Extracranial Suboccipital Region.*

An infant, aged 1 month, was referred by Dr. W. P. McDowell, of Norfolk, Va., because of a lump in the back of the head, presumably an occipital meningocele (figs. 22 and 23). The tumor had been present since birth and was then about double the size at birth. The whole head had also been rapidly increasing in size during the three weeks before operation. Before this time, the head had not

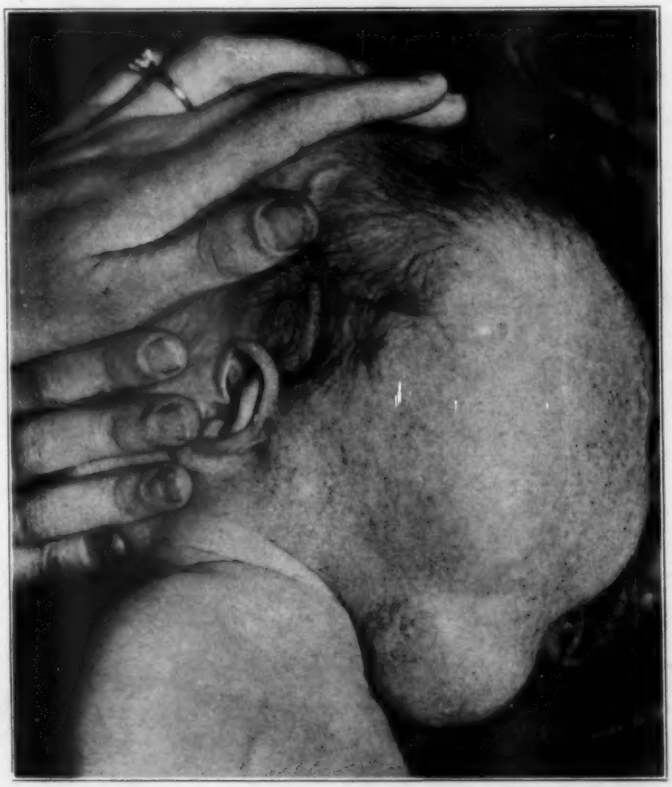

Fig. 22 (case 21).—Photograph of patient with a large extracranial and intracranial cavernous angioma. The position of the tumor suggested an occipital meningocele.

seemed unusually large. Convulsions had not occurred, neither had there been nausea or vomiting. The swelling was exactly in the midline in the suboccipital region; it was of oval-shape and measured about 5 by 5 by 7 cm. It was everywhere covered by normal skin, and did not show any evidence of nervous tissue. It was compressible and seemed to pulsate. At the time of operation, the diagnosis of meningocele was made, though doubtless had the light transmission test been made it would have changed this diagnosis. X-ray examination would also have excluded a meningocele, for there was no opening in the center of the occipital bone. Advanced obstructive hydrocephalus was diagnosed by ventricular estimation.

Operation.—At operation, the lesion was quickly recognized as a tumor. It was intimately attached to the skull and was so bloody that at every attempt to separate it from the skull applications of wax were necessary to stop bleeding. The periostium was everywhere absent, the bone rough and irregular from the extensive adherence of the tumor and the many vascular channels which penetrated it. Nowhere was an opening seen to penetrate the bone. For this reason, it was evident that the tumor was not causing the hydrocephalus. It was equally evident that another tumor, presumably of the same angiomatous type, must be present in the posterior cranial fossa, and causing the hydrocephalus. Necropsy proved this assumption to be correct. An equally large tumor was present in the posterior

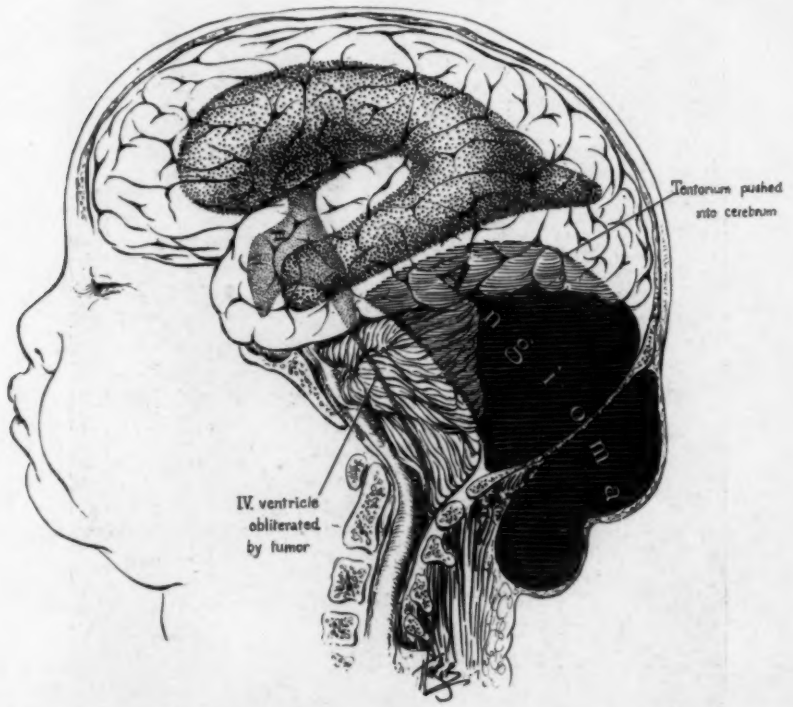

Fig. 23 (case 21).—The position and relative size of the tremendous angioma shown in figure 22. The tumor pushed the cerebellum far forward thereby causing the tentorium to bulge. It has completely occluded the fourth ventricle causing a hydrocephalus of high grade.

cranial fossa. It was attached to the inner surface of the occipital bone, and lay immediately beneath the external tumor. The internal and external tumors were directly continuous through the bone by angiomatous extensions of microscopic size.

Both intracranial and extracranial tumors were alike; they were soft, spongelike and compressible. Blood could be expressed from the spaces which were of varying size up to nearly 1 cm. in diameter.

The microscopic appearance showed the tumor to be a cavernous hemangioma.

CASE 22.—*Cavernous Angioma of Left Cerebellar Lobe.*

A well nourished woman, aged 35, was referred by Dr. Walter B. Martin, of Norfolk, Va., with the diagnosis of an unlocalized tumor of the brain. Her symptoms had begun ten years before when during a pregnancy she had had severe headaches in the frontal and temporal regions of both sides. The headache had shifted slowly to the back of the head. Since this time, she had had headaches of the same character about every six months; each attack lasted about from six to eight weeks. The headaches began gradually, increased steadily, reaching a maximum usually in about six weeks. She was then forced to stay in bed. They then disappeared gradually. The disappearance of the headaches could not be accounted for any more than their beginning. Nausea and vomiting accompanied

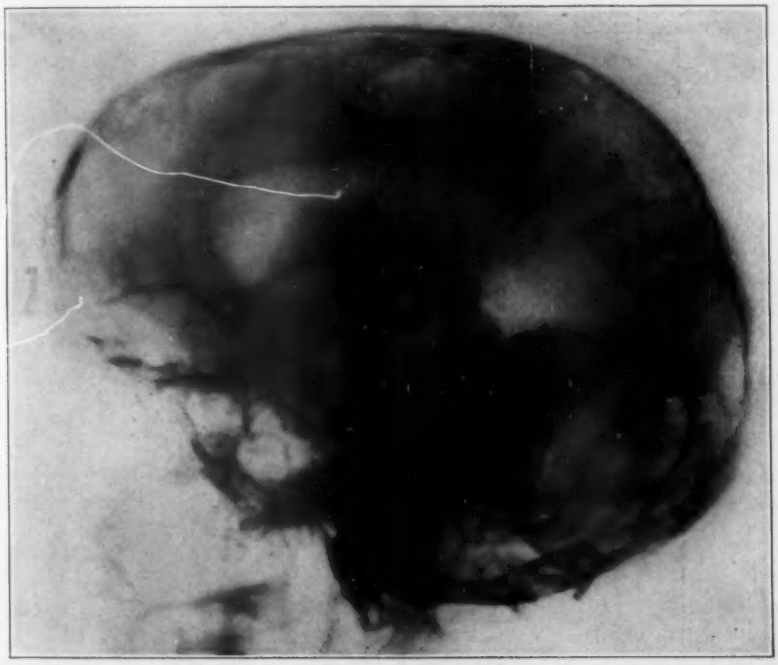

Fig. 24 (case 22).—Lateral ventriculogram. This patient had signs and symptoms of intracranial pressure, but none of the tumor's location. The ventriculogram shows greatly enlarged lateral and third ventricles.

the headaches. During one of these attacks of headache, she had partially lost the hearing in the left ear. Eight months before operation, in one of these spells, she had lost the sense of smell and taste, and since then had constantly smelled a nauseating odor of "burnt celluloid." Her last attack of headache had begun about twelve weeks before operation and persisted until that time. In this attack she felt some numbness in the left arm and leg and stiffness in the neck. There was no diplopia.

Neurologic examination showed the following positive conditions: (1) double choked disk, about equal on the two sides; (2) complete loss of smell; (3) 50 per cent loss of hearing—bone and air conduction in left ear.

It is noteworthy that except for a subjective cervical rigidity and the possible disturbance of hearing, there were no indications of a cerebellar lesion. The loss of smell and the possible uncinate attacks suggested a lesion in the uncinate gyrus (temporal lobe).

Ventriculography showed a bilateral hydrocephalus with a large third ventricle (figs. 24 and 25).

Operation.—On Dec. 29, 1925, cerebellar exploration was performed. A tumor appeared in the left cerebellar lobe. It reached the surface beneath the lateral sinus, to which it was attached by filmy adhesions. Two tortuous veins passed over the cerebellum and entered the tumor. A large artery also passed into the tumor from below. A third vein skirted the tumor. After the vessels on the surface of the cerebellar lobe had been tied, the tumor was removed by resecting

Fig. 25 (case 22).—Anteroposterior ventriculogram of the same patient. The symmetrical, dilated lateral ventricle and the mesially placed third ventricle (also enlarged) indicate the position of the tumor to be in the posterior cranial fossa.

a good margin of cerebellar tissue around it (figs. 26 and 27). The subcortical part of the tumor was not seen at any time until the resected mass was sectioned for study. The tumor was then seen to be composed entirely of a meshwork of blood-containing spaces with some interposed connective tissue. A diagnosis of cavernous angioma was made.

The postoperative course was uneventful. The patient did not suffer any noticeable ill effects of the loss of the cerebellar tissue. She has remained well to date, over two years after operation.

Case 23.—*Cavernous Angioma of the Fourth Ventricle.*

A healthy looking man, aged 31, was referred by Dr. Samuel Key of Austin, Tex. Two years before admission to the hospital, his right leg had occasionally

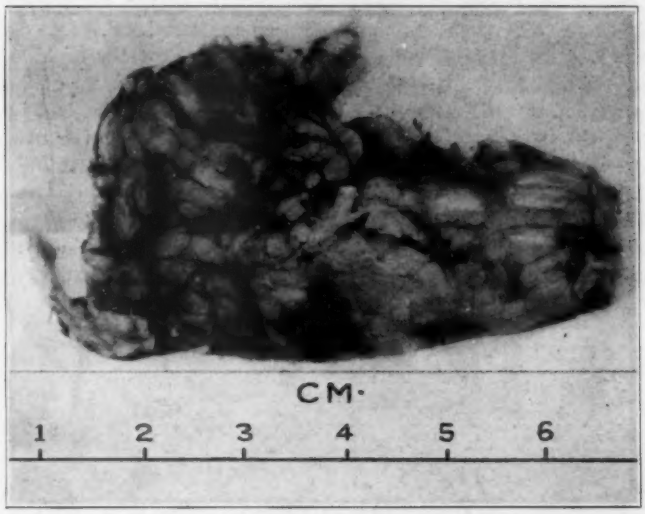

Fig. 26 (case 22).—Cavernous angioma removed with an area of cerebellar tissue surrounding it. The tumor has just reached the surface of the cerebellum at a point near the middle of the resected mass.

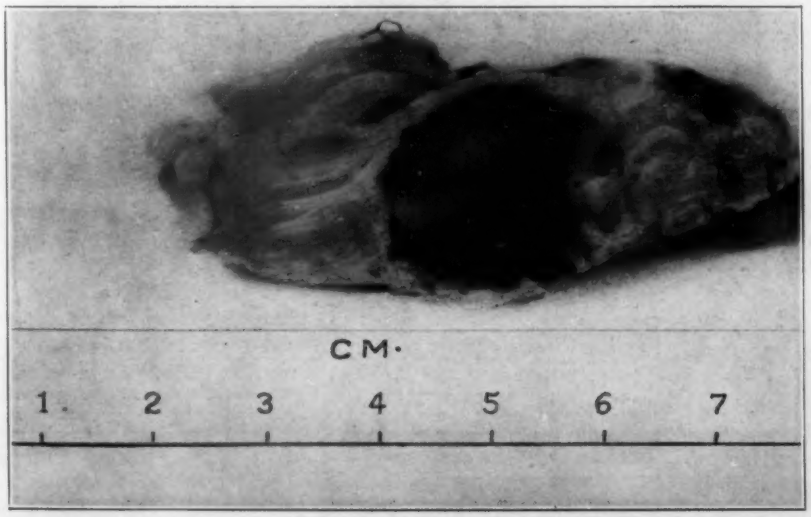

Fig. 27 (case 22).—Cross-section of resected cerebellar tissue and the tumor shown in figure 26.

dragged and become stiff. For seven or eight months, there had been some weakness in the fingers of the left hand. The fingers on the right hand had also become numb and stiff, but less than those on the left hand.

Six months before operation he had begun to have attacks of blurred vision; since this time, he had had several such attacks daily. Dimness of vision would last half an hour or more after each seizure. Later his vision had been greatly limited "on both sides." He had never had headache, but in the morning when getting up there had frequently been pain back of the right ear. When he held his neck stiff, this pain seemed to disappear.

About four months before operation, he had suddenly fallen to the floor unconscious. When he awakened, he was in bed but felt well. He did not bite his tongue and was not incontinent. Three weeks before operation, he had had a similar attack. He did not know whether he had had a convulsion.

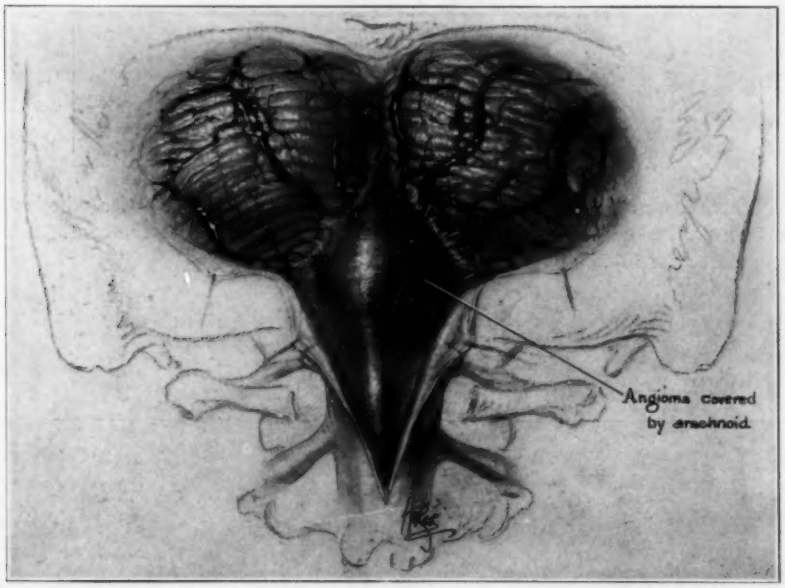

Fig. 28 (case 23).—Bulging tumor between the cerebellar lobes and over the medulla. It is covered with arachnoid which must be split before the tumor can be exposed.

The positive neurologic observations were: (1) bilateral choked disk (4 diopters in each eye); (2) visual fields greatly reduced; visual acuity 20/100 in each eye; (3) definite motor loss in left arm and leg; (4) definite hypo-esthesia in left arm and leg; (5) uncertain gait, but not staggering (Romberg sign negative); (6) slight nystagmus in right lateral fixation. It is noteworthy that all of the reflexes were normal. The x-ray picture showed destruction of the posterior clinoid processes.

Ventriculography showed high grade bilateral hydrocephalus with large third ventricle (figs. 31 and 32).

Operation.—On July 28, 1927, bilateral cerebellar operation was performed. A strictly midline tumor was found between the cerebellar lobes and resting directly on the medulla and pons (fig. 28). When first seen, it was covered with arachnoid

and was thought to be a glioma, but after the membranes had been split, it was seen to be a well encapsulated tumor. There was an oval, smooth, bluish, fluctuant central mass closely attached to the brain stem. From this tumor, which had every appearance of a venous aneurysm (it did not pulsate and imparted no thrill), three large veins, larger than slate pencils, emerged (fig. 29). One vein came from the vault of the tumor and passed over the right side of the pons and was lost to view; the second emerged from the vault of the tumor and passed over to the left side of the medulla, and the third passed from the lower pole of the tumor, down the center of the spinal cord and at the level of the axis (the atlas had been removed posteriorly), two branches passed over the right side of the spinal cord and one over the left. All of these veins were carefully ligated, after which the central tumor mass was carefully elevated from its bed in the brain stem (fig. 30). One other vein, slightly smaller than the one already mentioned, emerged from the exact center of the under surface of the tumor and passed directly into the medulla near its junction with the pons (fig. 30).

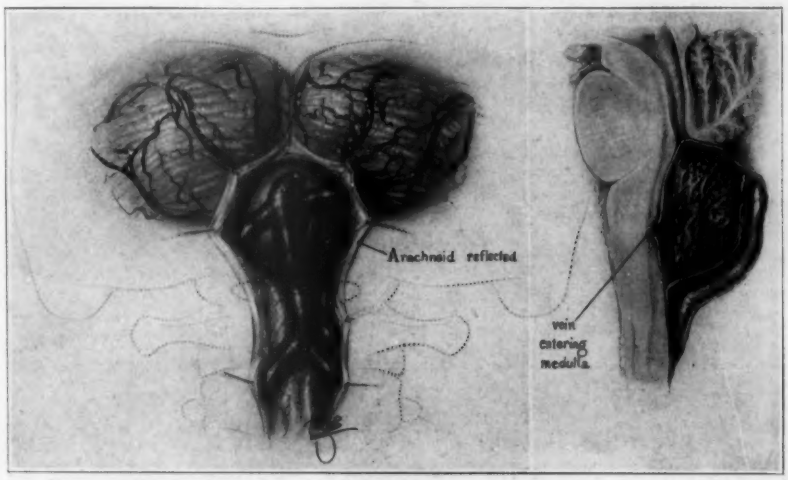

Fig. 29 (case 23).—Tumor exposed after splitting the arachnoid. The large veins issuing from the tumor suggested at first that the tumor was a venous sac (venous aneurysm). The five large veins which emerged from the tumor were ligated with silk; the tumor was then lifted upward and dissected from the brain stem to which it was loosely attached.

The patient promptly recovered from the operation which was without incident, except that there was some increase in the incoordination in the left hand. This disturbance soon improved, and when seen seven months later he was perfectly well except for a very slight weakness—far less than in the left hand on admission.

Case 24.—*Cavernous Angioma of Occipital Lobe with Hemorrhages.*

A normal looking man, aged 32, was referred by Dr. T. P. Sprunt, of Baltimore, in October, 1926. In February, 1926, the patient had had a spell of severe pain in the legs and arms, more on the left side. The pain had not been constant, but had occurred in waves. He had continued at work for ten days, when persistent nausea and vomiting had developed. He could not retain food.

After two weeks in bed, he had felt well enough to be up and about, but for five months he had felt groggy and tired. He had then returned to work. A month later, when arriving at the office, he had suddenly had an attack of severe vertigo, and two hours later had experienced violent nausea and vomiting, all of which had lasted for twelve hours; objects had seemed to whirl about him. Diplopia had also appeared at that time. There had been a queer feeling in the eyes, and his neck had been stiff. He said that he thought he had staggered at times, but that the dizziness may have accounted for this. He had improved gradually, and eight days later had again left the bed. For the next year and a half, he had done little work and had rested a great deal.

He had again been referred by Dr. Sprunt, in March, 1928, because bilateral choked disks had been discovered. He did not complain of headaches and felt

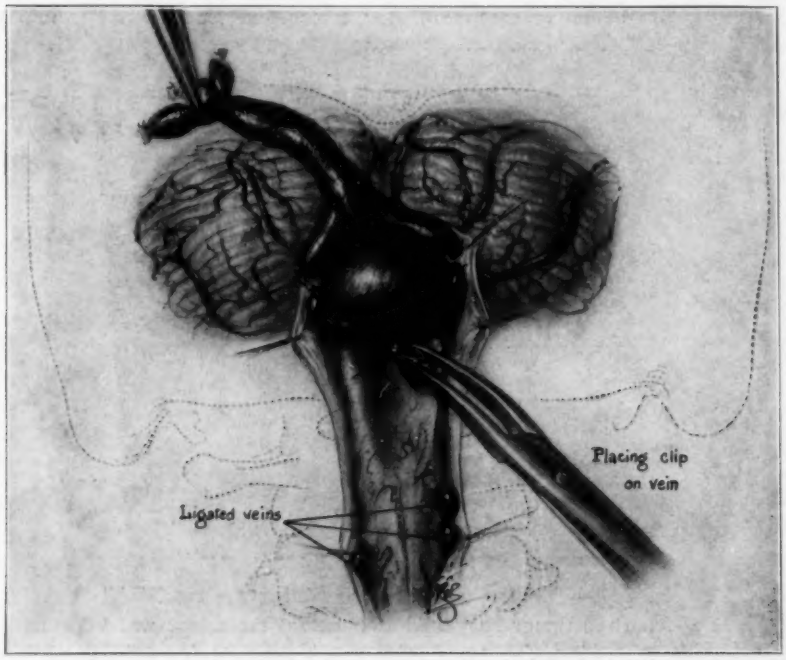

Fig. 30 (case 23).—Operative removal of tumor shown in figures 28 and 29. On elevating the tumor a single large vein passed into the medulla precisely in the midline. This vein was occluded with a silver clip and, after the division of the vein above the clip, the tumor lifted out in its entirety. Throughout the dissection of the tumor no artery of size was seen to enter it. There was practically no bleeding during the removal of the tumor.

that his recovery, though not complete, had been steadily progressive. He said that the dizzy feeling was still present when his head was suddenly turned to the right.

Except for a bilateral papilledema of 4 diopters in each eye, the results of the physical and neurological examinations were negative. It was my impression that the patient had a tumor of the brain, probably a cyst with an intracystic papilloma. The long duration of the symptoms with periods of marked improvement would

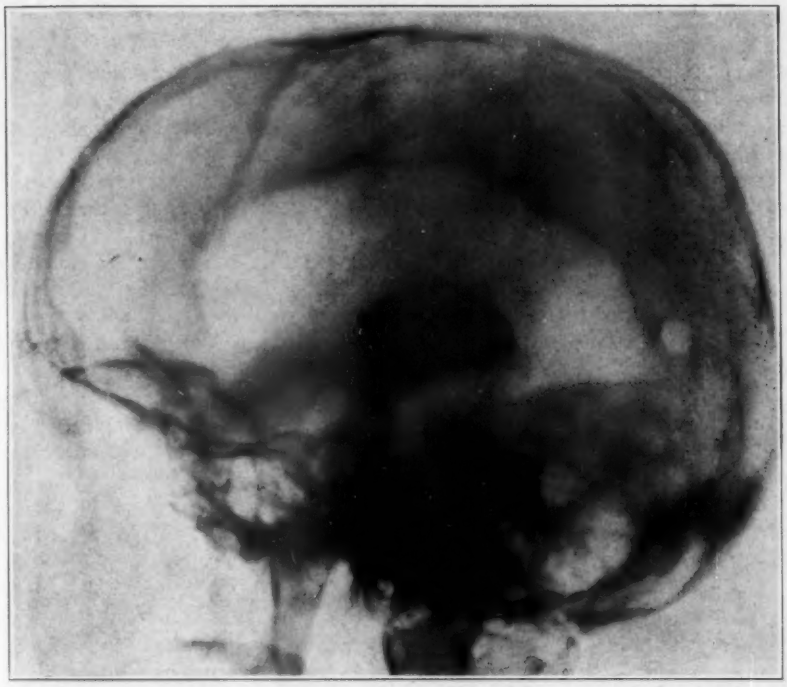

Fig. 31 (case 23).—Ventriculogram of tumor shown in figures 28, 29 and 30. It was situated far enough anteriorly to block the foramina of Luschka and produce a big hydrocephalus. Doubtless the block was of ball-valve character, for the tumor must have been present since birth. The patient is now 31 years old.

Fig. 32 (case 23).—Same as figure 31.

seem to indicate a cyst. The sudden symptoms on several occasions suggested hemorrhages from the tumor. Because of the rigidity of the neck and the outspoken dizziness,[3] particularly on turning the head to the right, a presumptive localization of the tumor was made in the cerebellum.

An injection of air into the cerebral ventricles was advised for the accurate localization of the tumor, to be followed by the exploration of the tumor in anticipation of its removal if possible.

The patient was scheduled to enter the hospital a week later, on March 17, 1928. Suddenly, on March 16, 1928, he complained of violent dizziness and headache. A few minutes later, he was deeply comatose and had Cheyne-Stokes respirations. He was rushed to the hospital, but became cyanotic and died as he entered the operating room. In an attempt to resuscitate him, a ventricular puncture was performed quickly in first aid fashion. A spurt of dark blood (hemorrhage) followed the right occipital puncture, but his pulse did not beat again and respiration did not commence. It was then clear that he had had a cerebral hemorrhage in the right occipital lobe.

Necropsy showed a large, oval cavity (as large as one's fist) in the right occipital lobe and extending into the temporal lobe (fig. 33). The cyst was about

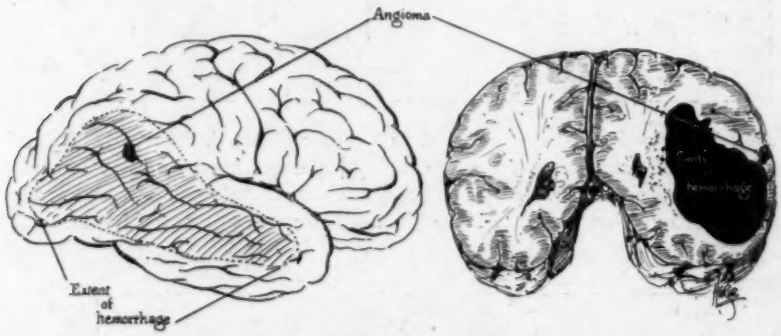

Fig. 33 (case 24).—Sketch of the brain (at necropsy) showing the position and extent of a large hemorrhage and small angioma. This patient died before operation.

from 1 to 2 cm. below the surface of the brain. At first a tumor could not be seen, but on more careful inspection, a small, smooth swelling was noted in the region of the angular gyrus. At first it was thought to be merely the indentation of a convolution, but cross-section demonstrated a small mass of loose, spongy tissue measuring about 1 by 1 cm.; it replaced the cortex and connected with the pia-arachnoid (fig. 34). It was clearly an angioma.

The microscopic diagnosis was cavernous angioma.

Relationship of Angiomas of the Brain to Angiomas and Other Congenital Lesions Elsewhere in the Body.—The frequency of multiple angiomas in the brain must prepare one to believe that the same lesions

3. This case was recently reported in a paper dealing with dizziness in Ménière's disease, brain tumors and other lesions, as an example of this type of dizziness associated with tumors located elsewhere than in the posterior cranial fossa. (Arch. Surg. **16**:1127 [June] 1928).

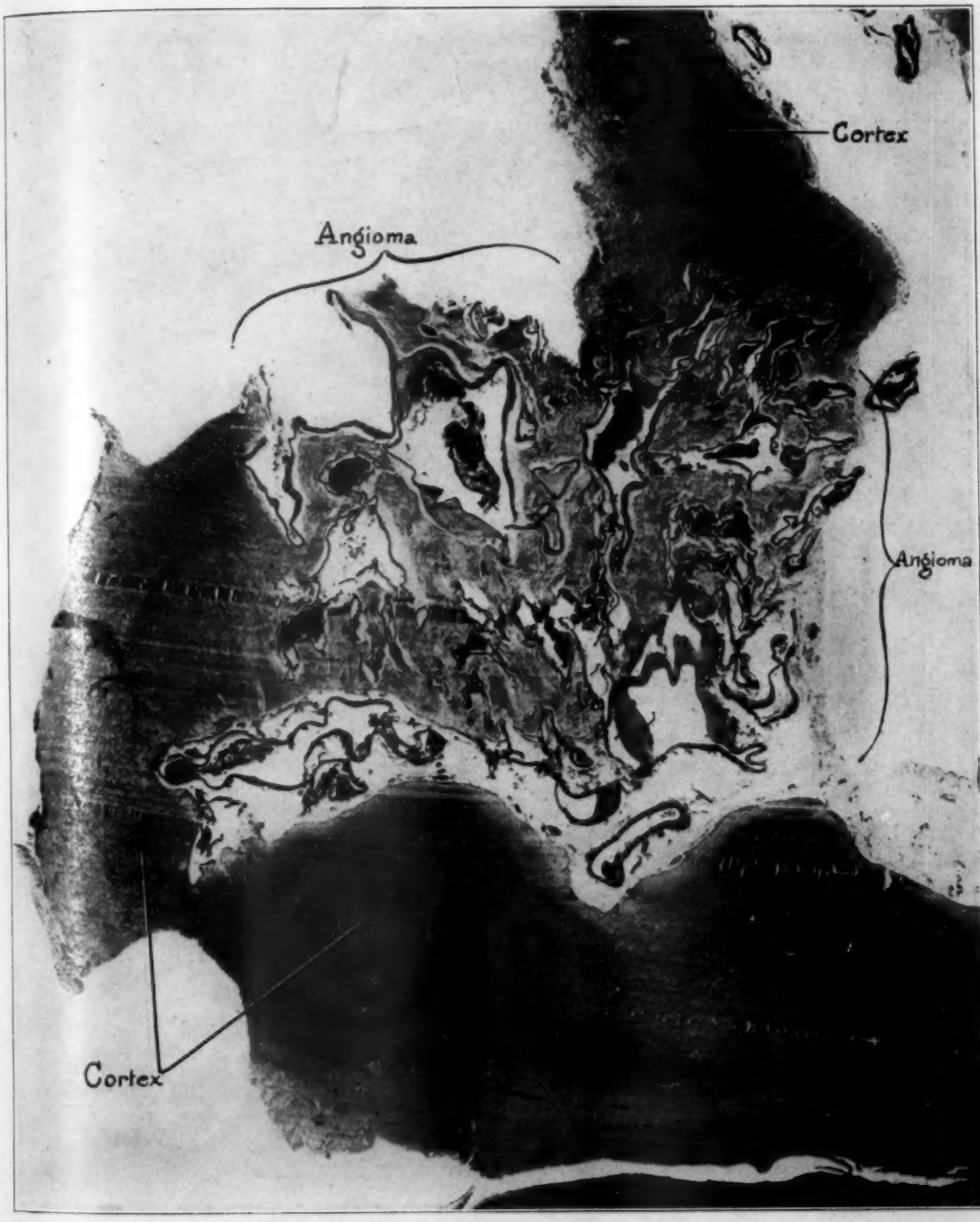

Fig. 34 (case 24).—Photomicrograph (low grade) showing relationship of an angioma to the cortex in an occipital lobe. To remove an angioma of this character it is necessary to include the cortex just beyond its border. This also makes its extirpation much easier because the vascular tumor is avoided. Spontaneous hemorrhage is always a danger, even in a seemingly insignificant and dormant angioma.

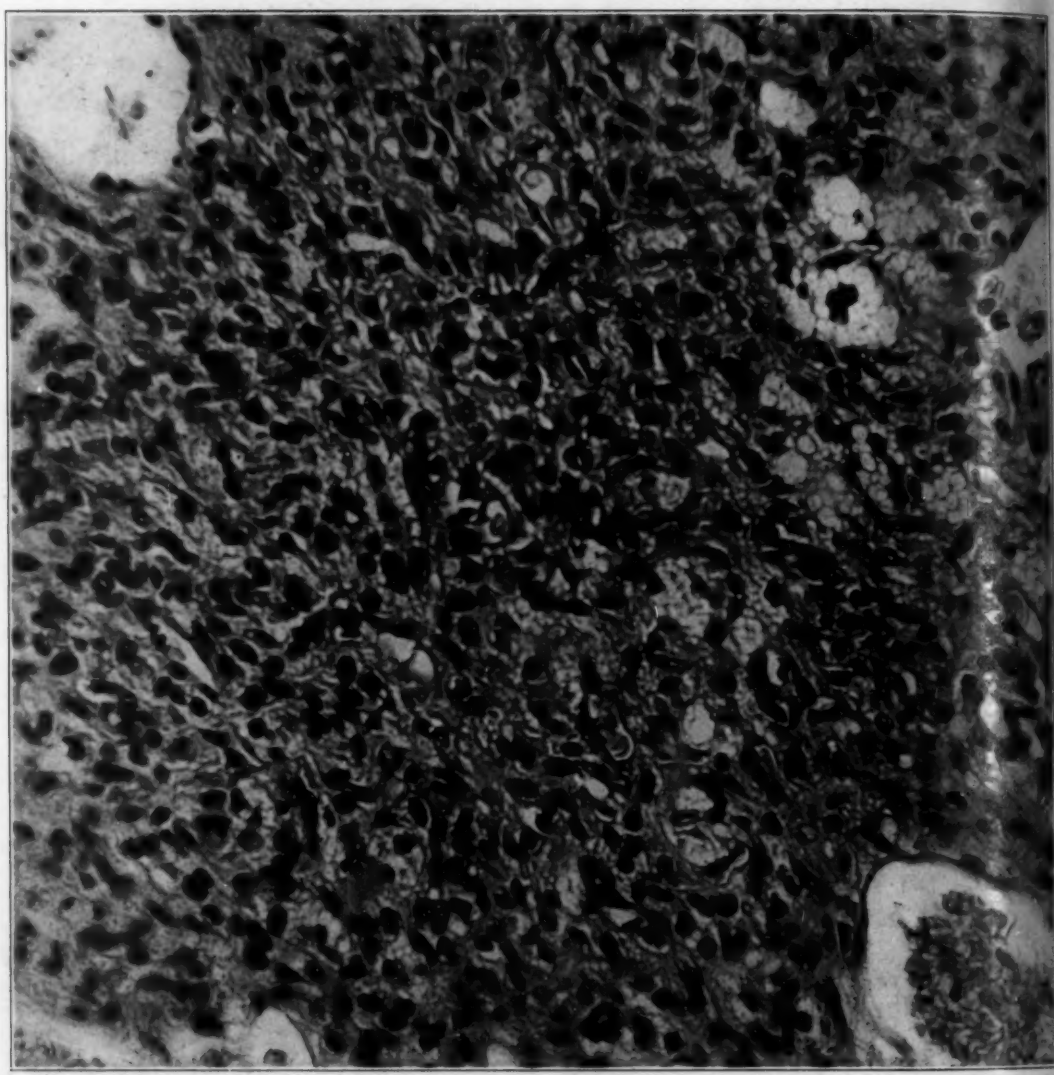

Fig. 35.—Photomicrographs in figures 35 to 45 are taken from cases of angiomas in cysts and cavernous angiomas. This figure is from case 13.

Fig. 36.—Case 14.

Fig. 37.—Case 15.

Fig. 38.—Case 16.

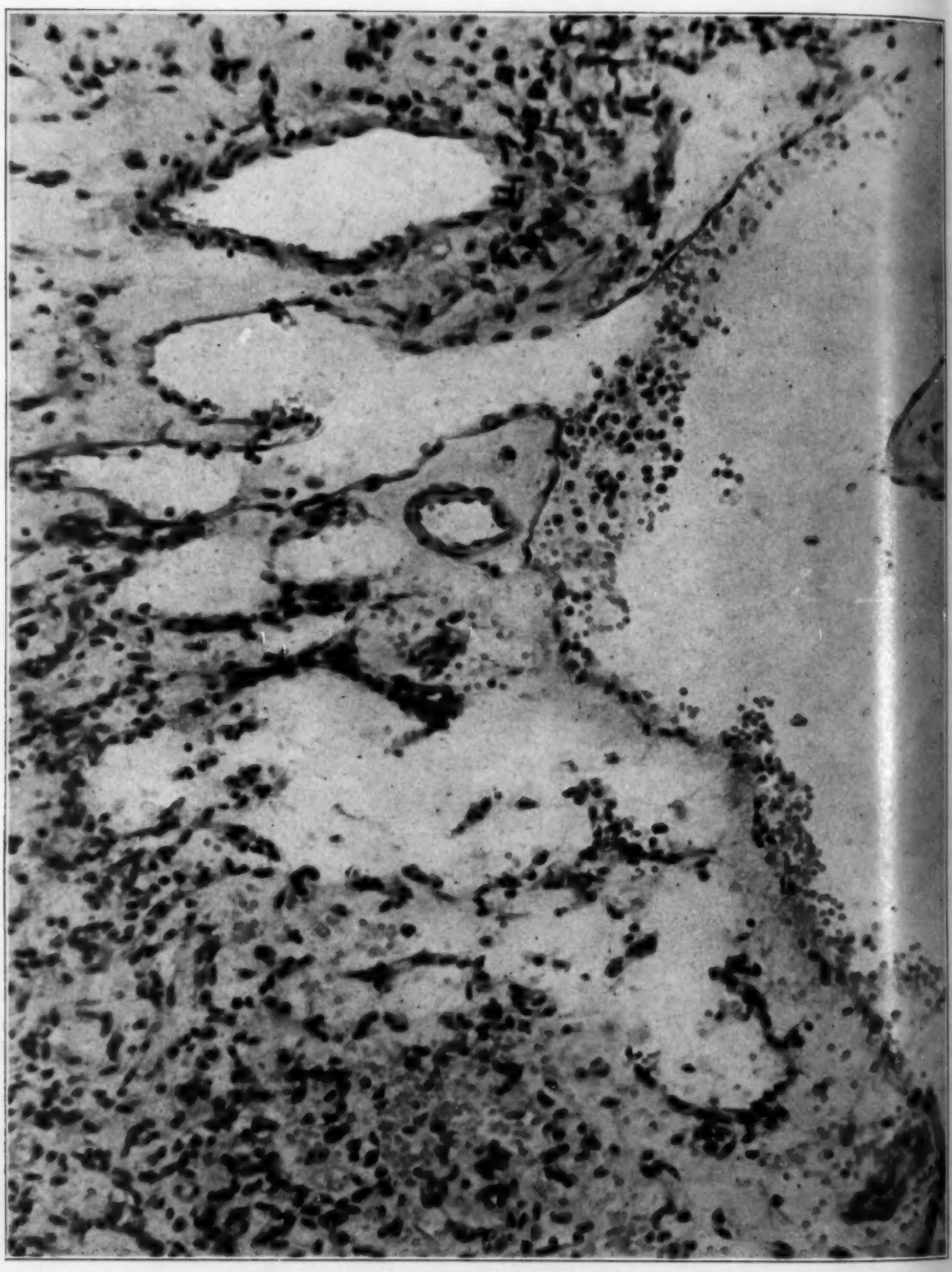

Fig. 39.—Case 17.

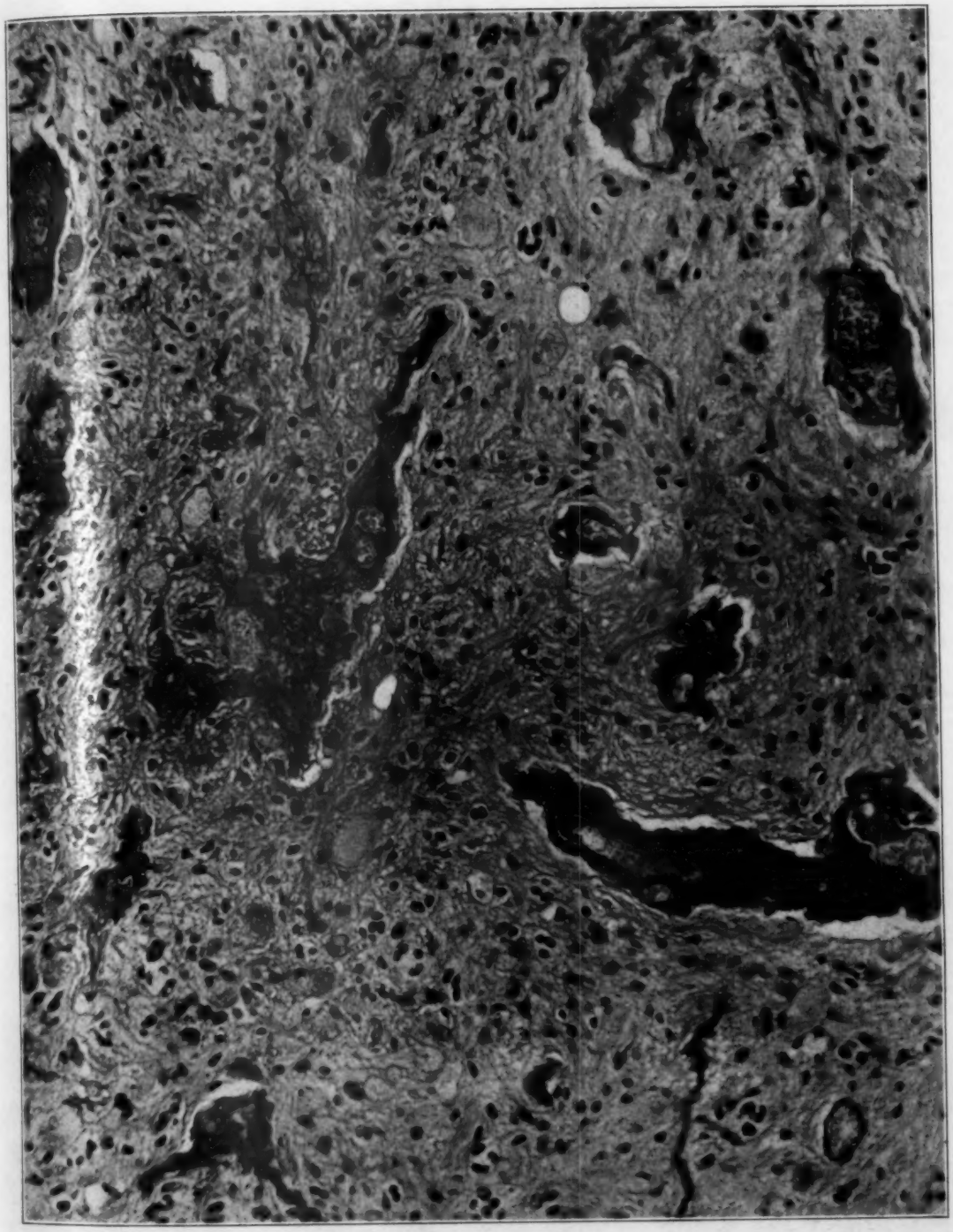

Fig. 40.—Case 18.

Fig. 41.—Case 19.

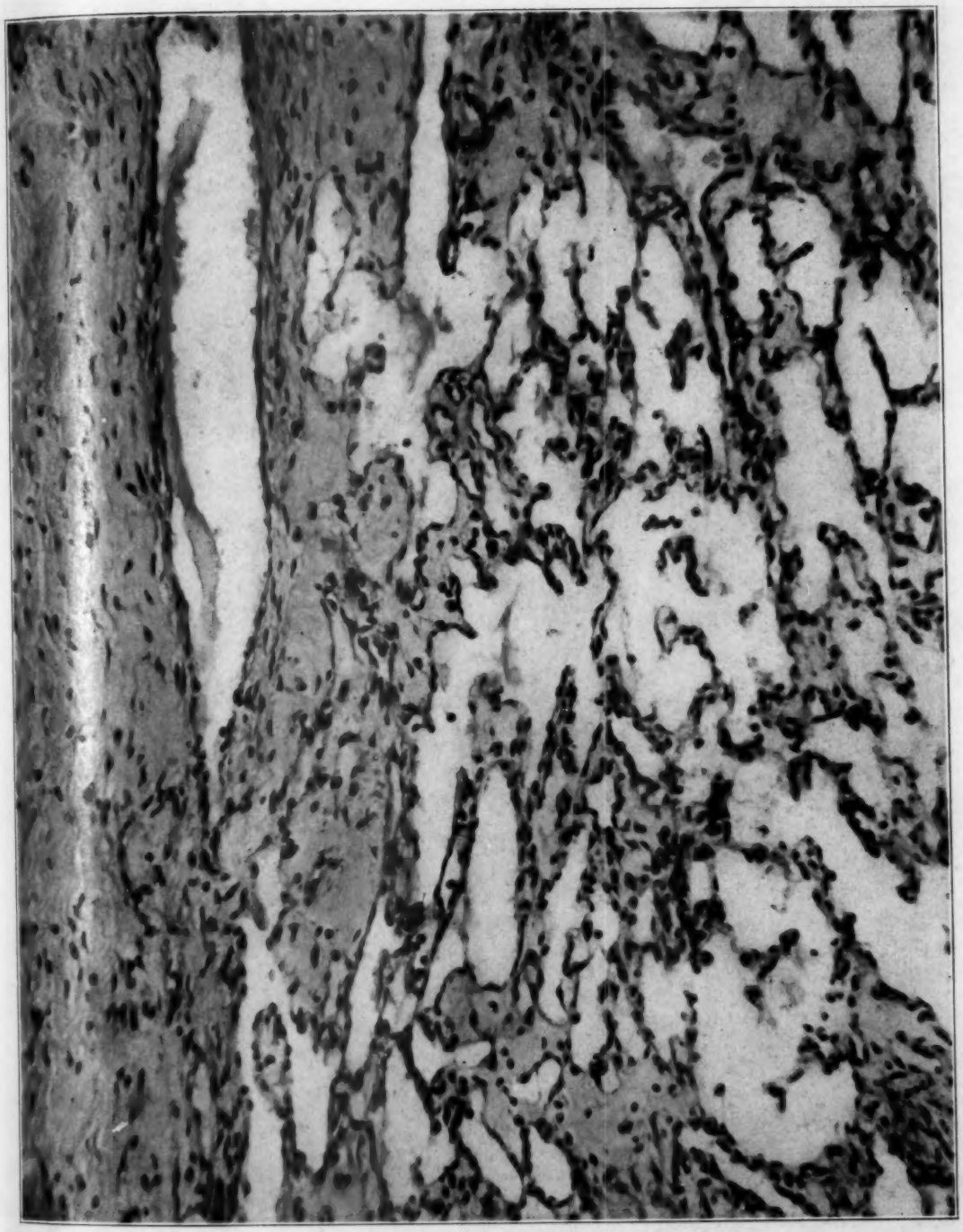

Fig. 42 (case 21).—Showing invasion of the dura by the tumor.

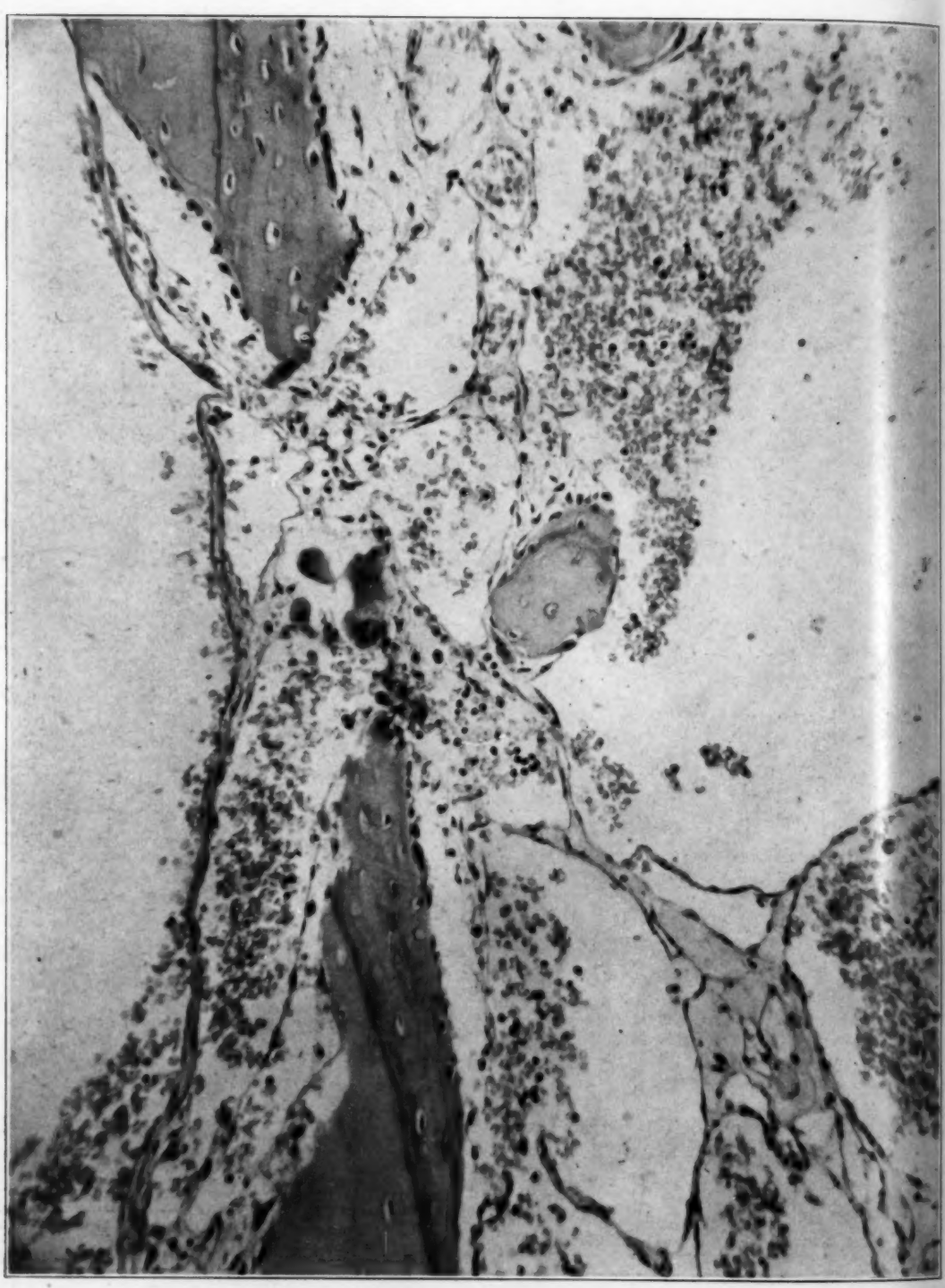

Fig. 43 (case 21).—Showing perforation of the bone by the angiomatous spaces.

Fig. 44.—Case 22.

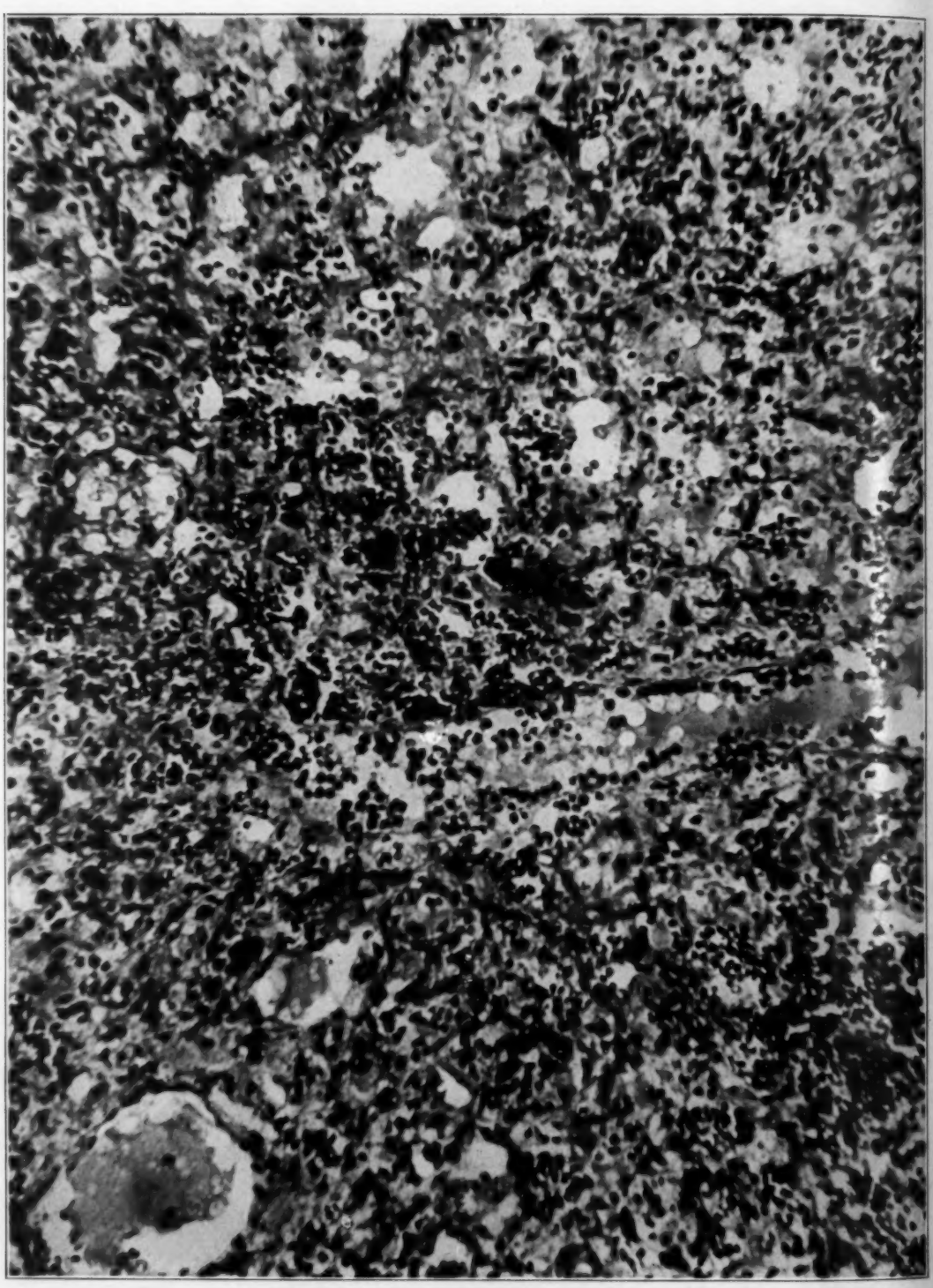

Fig. 45.—Case 23.

must occur concomitantly elsewhere in the body, especially when it is recognized that these lesions are peculiar to the vascular system and not to the brain. Strominger (1903) demonstrated one of the early cases of cavernous angioma of the brain and called attention to an associated extensive nevus of the face which he considered highly significant. Finkelnburg's (1905) patient had a cyst of the cord in addition to angiomas of the corpora quadrigemina and fourth ventricle. Koch's (1913) patient had diabetes mellitus, and at necropsy, cysts of the pancreas, cavernous angiomas of the liver, an angiomatous cyst of one cerebellar lobe and a cavernous angioma of the other lobe were found. In addition, his patient had von Hippel's disease, i.e., so-called angiomatosis retinae. This was the first instance of the association of the vascular lesion in the retina (assumed to be an angioma) and an angioma of the brain. In 1913, Oppenheim presented to the medical society four patients, in each of whom he suspected an angioma of the brain because congenital nevi of the face and body existed in association with long-standing symptoms of cerebral origin, mainly paralyses and convulsions. Although none of his diagnoses were checked by necropsy or operation, Oppenheim said, "An angioma of the brain must always be considered when vascular naeve of the face are present." Berblinger (1922) reported another case of von Hippel's disease in a patient who had a cavernous angioma of the body.

The association of angiomatosis of the central nervous system with angiomatosis retinae (von Hippel's disease) and cysts of the pancreas, liver and spine attained new importance with Lindau's splendid publication. He thinks that cysts or cavernous angiomas in the cerebellum occur in 20 per cent of all cases of angiomatosis retinae. In half of his cases of angiomatous cysts of the cerebellum, there were cysts of the pancreas; and in two-thirds, cysts of the kidneys. Lindau considered these disturbances of the brain, retina, pancreas and kidneys a congenital maldevelopment complex. Since Lindau's publication, Schuback (1927) and Wohlwill (1927) have published reports of cases of angiomas of the brain in which cysts of the spinal cord, pancreas and kidneys and angiomatosis retinae existed. Kufs (1928) reported a remarkable case of angioma of the brain with nevi of the body and many cavernomas of the liver. This patient's daughter had had a cerebral hemorrhage (from which she had recovered) at the age of 17. Kufs looked on this hemorrhage as a rupture of an angioma, and thought that the family indicated a hereditary basis for the angioma.

In none of my cases has von Hippel's disease been observed, although the eyegrounds have always been carefully examined. The retinal picture is so striking and characteristic that, once seen, it could not be missed. As most of the pathologic material was obtained at operation,

nothing can be contributed toward a better knowledge of the relationship between angiomas of the brain and cysts of the abdominal organs.

SUMMARY AND CONCLUSIONS

1. A series of cases of venous anomalies, plexiform angiomas, angiomatous cysts and cavernous angiomas of the brain are reported. The additional cases of similar types are collected from the literature, and their clinical features are analyzed.

2. The venous anomalies are of congenital origin. Their clinical symptoms are usually epilepsy and disturbances of mentality. They are frequently associated with other deformations of the brain.

3. Three cases of angioma plexiforme are reported. They resemble a similar lesion well known in the spinal cord.

4. A network of venous spaces in the dura and communicating freely with the longitudinal sinus is offered as a cause of focal epilepsy beginning in the leg or arm. Its constant location suggests that it is probably the congenital remains of an embryonic dural circulation.

5. Angiomatous cysts exist throughout the brain, but with greatest frequency in the cerebellum. The size of the tumor embedded in the wall of the cyst is relatively insignificant. Intracranial pressure develops rapidly because of the cyst formation and the resultant hydrocephalus. Localizing symptoms are usually, but not always, present. These tumors cannot be differentiated clinically from other types of cysts of the brain.

6. Cavernous angiomas assume many gross appearances. They are scattered throughout the brain, but appear to occur with greatest frequency in the frontoparietal region. The predominating symptom of this type of tumor is jacksonian epilepsy with or without transient or permanent motor weakness. Pressure symptoms will develop if the tumor is situated near the ventricular channels or outlets. The typical tumors begin early in life; they grow slowly, and the symptoms endure for many years. A clinical diagnosis can be made at times.

7. Hemorrhage from the tumor is always a potential danger in all types of angiomas, though to a less degree than in arteriovenous aneurysms of the brain.

8. Both the cavernous angiomas and the angiomatous cysts should be treated surgically by complete removal of the solid tumor together with a margin of contiguous brain tissue. Both of these types of tumor offer good prospects of complete cure and with relatively little risk. The tumors in the cysts are among the easiest tumors of the brain to extirpate.

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LIGATION OF THE TERMINAL ABDOMINAL AORTA

AN EXPERIMENTAL STUDY *

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The greater portion of the experimental investigation which has been conducted heretofore for the study of the effects of occlusion of the abdominal aorta has been concerned with the changes in the volume of flow of blood through the posterior extremities and with the development of a collateral circulation. The fact that death has so often followed obstruction of the abdominal aorta in man has been frequently ascribed to the effect of this procedure on the heart. The purpose of this study was primarily to observe the effects of occlusion of the abdominal aorta on the heart.

The importance of such a study is apparent from the consideration of the different views which have been expressed in two recent reports of successful ligation of the abdominal aorta. Matas [1] described the changes in a patient who lived for approximately one year after almost complete occlusion of the abdominal aorta. It is evident from this report that Matas believes that occlusion of the aorta produces important effects on the heart. He states:

> It is really surprising that the myocardium, enfeebled by a protracted and most virulent syphilitic infection, a generalized polyarthritis of the spine, hip and knee-joint, accompanied by a constant high fever for months, should have survived the continued strain of aortic and pulmonary obstruction imposed upon the heart by the total occlusion of the abdominal aorta.

More recently, one of us (B. B.[2]) reported a case in which the abdominal aorta was completely occluded for a period of three months. In discussing the effect of this procedure on the heart, it was stated:

> The heart was believed to be slightly enlarged before operation. At the time of death, three months after operation, the heart was found to be essentially normal. There was, therefore, no indication in this instance of the occlusion of the abdominal aorta affecting the heart in any way.

A similar difference of opinion has been expressed by two previous investigators who have studied this problem by experimental methods.

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2. Brooks, Barney: Ligation of the Aorta: Clinical and Experimental Study, J. A. M. A. **87**:722 (Sept. 4) 1926.

Kast,[3] from a series of experiments in which he studied the effect of obstruction of the aorta on the blood pressure, found that there was little, if any, change in the blood pressure in the artery proximal to the site of occlusion. From these experiments, Kast concludes that ligation of the abdominal aorta is not to be considered as endangering life from its effect on the heart. Katzenstein,[4] from a similar experimental study, found that occlusion of the abdominal aorta resulted in an elevation of the blood pressure in the artery proximal to the site of obstruction, and that animals having had the abdominal aorta obstructed for a considerable period of time showed dilatation and hypertrophy of the heart. From these experiments, Katzenstein concludes that obstruction of the aorta results in placing on the heart of the patient an extraordinarily great strain.

The basis of this paper is the observations of the effect of occlusion of the abdominal aorta on the blood pressure, the cardiac output and the distribution of the blood volume.

METHODS

Dogs were used in all experiments. For the operative procedure necessary for occlusion of the aorta, some form of anesthetic was always employed. Ether was usually given for the opening of the abdomen and isolation of the vessel. All of the observations on blood pressure were made on dogs anesthetized with morphine. Some of the determinations of cardiac output were made on dogs trained to submit to this procedure without anesthetic. The blood pressure was determined by placing cannulas, which were connected with mercury manometers, in the carotid and femoral arteries. The cardiac output was calculated from the determination of the oxygen content of samples of blood from the right and left heart, taken during a period in which the consumption of oxygen was measured. The consumption of oxygen was determined by a Benedict spirometer with the graphic recording device. The animal was connected with the spirometer either by the use of a specially constructed mask which fitted tightly over the mouth or by a tube placed in the trachea. Specimens of blood for gas analyses were withdrawn with the usual precautions from the right and left ventricles. The oxygen and the carbon dioxide of the specimens of arterial and venous blood were determined by the use of the Van Slyke-Neill[5] manometric apparatus. The circulatory minute volume was calculated from the Fick formula:

$$\frac{\text{Cc. } O_2 \text{ consumed per minute}}{\text{Amount of } O_2 \text{ taken up in lungs by 1 cc. of blood}} = \text{Number of cubic centimeters of blood flowing through lungs per minute.}$$

In all experiments in which the animals were to be studied for long periods, an aseptic operative technic was employed, and the complete obstruction of the abdominal aorta was made certain by the division of the vessel between ligatures or the careful examination of the vessel at autopsy. In all experiments in which the effect of the occlusion of the aorta on the cardiac output was determined, one or more control determinations of the cardiac output were made previous to the institution of any other experimental procedures.

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4. Katzenstein, M.: Arch. f. klin. Chir. **76**:581, 1905.
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The following possible objections to the experimental method require discussion: (1) the influence of the anesthetic and (2) the influence of the operative procedure necessary for the occlusion of the aorta. In regard to the anesthetics used, the possible influence of morphine on the cardiac output was controlled by the studies on the trained animals in which anesthetic was not used. In these experiments, the cardiac output was determined without any anesthetic. The animal was then given an anesthetic and the aorta occluded. The cardiac output was subsequently determined after recovery without any anesthetic. As regards the effect of ether anesthesia, in other experimental work not included in this paper, one of us (A. B.) has shown that the administration of ether in an amount comparable to that used in these experiments always results in an increase in the cardiac output. An example of an experiment showing the influence of ether on the cardiac output is given in table 1. It has already been adequately established that neither of the

TABLE 1.—*Effect of Ether Without Operation on the Cardiac Output*

Date	Weight, Kg.	Pulse Rate, per Minute	Temperature, F.	Arterial O_2, per Cent by Volume	Venous O_2, per Cent by Volume	Arterial Venous Difference per Cent by Volume	Oxygen Capacity, per Cent by Volume	Saturation, per Cent	O_2 Consumption, Cc. per Minute	p_H	Cardiac Output, Cc. per Minute	Output per Kg., per Minute, Cc.	Output, per Beat, Cc.
5/12/26 Control study, ¾ grain morphine	8.6	70	99	15.33	8.88	6.48	17.1	90	73.95	7.35	1141	132.7	16.3
5/12/26 After ether for 7 minutes	8.6	150	99	14.04	11.04	3	17.22	82	59.04	7.29	1968	228.9	13.1
5/12/26 After additional ether.	8.6	150	99	14.40	11.40	3	.....	..	58.4	7.30	1947	226.4	13.0
5/12/26 2 hours after stopping ether	8.6	76	98.5	15.24	8.66	6.58	.....	..	75.64	7.36	1148	133.4	15.1

Protocol: 5/12/26, control study performed after giving ¾ grain of morphine. Dog then given ether anesthesia through a mask seven minutes until the eye reflexes were barely abolished, and a determination of the output made. The ether was discontinued for a few minutes and then the animal was again given an anesthetic for seven minutes and another determination of the output made. The last studies were made two hours after the ether was discontinued. Animal was quiet during all the observations.

drugs used as an anesthetic in the amounts used in these experiments causes any appreciable alteration in blood pressure. The possible influence of the operative procedure necessary for ligation of the aorta was controlled by determinations of the cardiac output and blood pressure in five experiments in which the abdomen was opened and the aorta isolated without being occluded. This procedure was usually followed by a definite increase in the cardiac output and produced only temporary changes in the blood pressure. The results of these experiments are shown in tables 2 and 3.

RESULTS

It is obvious that it is impossible to make observations on both the blood pressure and the cardiac output on a single animal for more than a relatively short period of time by the methods used in this study. In most of the experiments, therefore, the effects of occlusion of the aorta on the blood pressure and on the cardiac output were

studied separately. In four experiments, however, the blood pressure was recorded continuously and the cardiac output determined repeatedly for periods as long as the general condition of the experimental animals could be maintained sufficiently well to make the observations of value.

TABLE 2.—*Effect of Exposure of the Aorta Without Ligation on the Cardiac Output*

Date	Weight, Kg.	Pulse Rate, per Minute	Temperature, F.	Arterial O_2, per Cent by Volume	Venous O_2, per Cent by Volume	Arterial Venous Difference, per Cent by Volume	Arterial CO_2, per Cent by Volume	Venous CO_2, per Cent by Volume	O_2 Consumption, Cc. per Minute	Cardiac Output, per Minute, Cc.	Output per Kg., per Minute, Cc.	Output per Beat, Cc.
10/8/26 Control study, no morphine	14	120	103.2	19.98	14.41	5.57	45.16	50.63	131.6	2362	169	20
10/8/26 4 hours after operation, no morphine	14	140	103.4	20.82	13.93	6.85	45.62	47.98	162.0	2364	169	17
10/9/26 28 hours after operation, no morphine	14	128	102.8	19.37	12.71	6.66	45.90	52.86	154.3	2317	166	19

Protocol: 10/8/26, healthy young male dog, control studies without morphine at 3:30 p. m. at 4: 30 p. m., under ether anesthesia, the distal abdominal aorta was exposed and isolated but not ligated, 9: 00 p. m., four hours after completion of operation, second studies were made. 10/9/26, twenty-eight hours after operation, studies made without morphine.

TABLE 3.—*Effect of the Cardiac Output of (1) Ether Anesthesia, and (2) Exposure of the Aorta Without Ligation*

Date	Weight, Kg.	Pulse Rate, per Minute	Temperature, F.	Arterial O_2, per Cent by Volume	Venous O_2, per Cent by Volume	Arterial Venous Difference, per Cent by Volume	Oxygen Capacity, per Cent by Volume	Saturation, per Cent	O_2 Consumption, Cc. per Minute	Cardiac Output, per Minute, Cc.	Output per Kg., per Minute, Cc.	Output per Beat, Cc.
6/1/26. 2 p. m. Control study, 1 grain morphine	9.1	65	100.4	13.95	6.2	7.75	15.32	91	77.49	909	110	15.4
6/1/26. 4: 30 p. m. After anesthesia for 40 minutes.....	9.1	130	98.4	11.92	6.79	5.13	.....	..	70.11	1367	150.2	10.5
6/1/26. 8: 45 p. m. 4 hours after anesthesia and operation..	9.1	150	98	14.88	9.12	5.76	.....	..	79.33	1377	151.3	9.2

Protocol: 6/1/26, 1: 30 p. m., 1 grain of morphine. 2: 00 p. m., dog completely quiet, control study. 4: 30 p. m., completion of forty minutes ether anesthetic. Eye reflexes abolished. 8:45 p. m., four hours following completion of anesthesia, dog able to walk around, but unsteady. Third determinations made.

The results of these four experiments are shown in tables 4, 5, 6 and 7, and in figures 1 and 2.

(a) The Effect on the Cardiac Output of Occlusion of the Abdominal Aorta.—In the study of the effect of occlusion of the aorta on the cardiac output, fifty-seven determinations of the cardiac output were

made on thirteen dogs. Three of these animals were trained so as not to require the administration of morphine. In five experiments, observations were made for only relatively short periods after the occlusion of the aorta. In eight experiments, the operative technic was

TABLE 4.—*Effect of the Cardiac Output and Blood Pressure of (1) Exposing Aorta, and (2) Ligating Aorta*

Date	Weight, Kg.	Pulse Rate, per Minute	Temperature, F.	Arterial O_2, per Cent by Volume	Venous O_2, per Cent by Volume	Arterial Venous Difference, per Cent by Volume	Arterial CO_2, per Cent by Volume	Venous CO_2, per Cent by Volume	Mean Carotid Pressure	Mean Femoral Pressure	O_2 Consumption Cc. per Minute	Cardiac Output, per Minute, Cc.	Output per Kg., per Minute, Cc.	Output per Beat, Cc.
11/2/26														
Control study, 1 grain morphine....	12.5	40	97	17.07	10.02	7.05	42.37	48.44	138	130	78.3	1111	89	28
10 minutes after exposing aorta	12.5	160	96.8	18.1	13.03	5.07	37.67	46.92	118	118	99.0	1953	156	12
10 minutes after ligating aorta	12.5	166	95	17.61	10.49	7.12	39.12	44.16	108	16	90.0	1265	101	8

Protocol: 11/2/26, 1: 00 p. m., 1 grain of morphine, 2: 00 p. m., control determinations. 2: 50 p. m., animal given few whiffs of ether, aorta exposed, cord which was not tied placed around it. 3: 10 p. m., studies with ligature untied. 3: 25 p. m., ligature tied. 3: 35 p. m., studies with ligature tied.

TABLE 5.—*Effect of the Ligation of the Abdominal Aorta on the Cardiac Output and Blood Pressure*

Date	Weight, Kg.	Pulse Rate, per Minute	Temperature, F.	Arterial O_2, per Cent by Volume	Venous O_2, per Cent by Volume	Arterial Venous, Difference per Cent by Volume	Arterial CO_2, per Cent by Volume	Venous CO_2, per Cent by Volume	Mean Carotid Pressure	Mean Femoral Pressure	O_2 Consumption Cc. per Minute	Cardiac Output per Minute, Cc.	Output per Kg., per Minute, Cc.	Output per Beat Cc.
11/3/26. 2 p. m.														
Control study, 1 grain morphine	8	56	97	20.16	15.0	5.16	40.37	42.70	154	144	59.1	1145	143	20
3: 00 p. m.														
20 minutes after exposing aorta	8	150	96.6	19.56	15.84	3.72	37.76	39.68	148	138	59.1	1589	199	11
3: 38 p. m.														
30 minutes after ligating aorta	8	165	95.4	20.28	14.76	5.52	34.33	40.30	134	...	66.8	1210	151	7
4: 08 p. m.														
1 hour after ligating aorta	8	165	95	20.04	11.88	8.16	35.01	40.36	102	22	66.8	819	124	5

Protocol: 11/3/26, 1: 00 p. m., 1 grain of morphine 2: 00 p. m., control study. 2: 35 p. m., few whiffs of ether, aorta exposed, ligature which was not tied placed around it. 3: 00 p. m., determinations. 3: 08 p. m., aorta occluded by ligature. 3:38 p. m., thirty minutes after occluding aorta, determinations. 4:08 p. m., one hour after occluding aorta, determinations.

carried out under aseptic conditions, and the animals were studied for periods of from one to twenty-one days. The results of all experiments are tabulated in tables 4 to 16.

From these results it is clear that in all experiments in which the cardiac output was determined not earlier than thirty minutes

nor later than twenty-four hours after the aorta was ligated, the cardiac output was decreased. In two instances in which there was a slight increase in the cardiac output during the first thirty minutes after

TABLE 6.—*Effect of the Ligation of the Abdominal Aorta on the Cardiac Output and Blood Pressure*

Date	Weight, Kg.	Pulse Rate, per Minute	Temperature, F.	Arterial O_2, per Cent by Volume	Venous O_2, per Cent by Volume	Arterial Venous Difference, per Cent by Volume	Arterial CO_2, per Cent by Volume	Venous CO_2, per Cent by Volume	Mean Carotid Pressure	Mean Femoral Pressure	O_2 Consumption, Cc. per Minute	Cardiac Output, per Minute, Cc.	Output per Kg., per Minute, Cc.	Output per Beat, Cc.
9/8/26														
1 grain morphine 10:45 a. m.; control study 11: 50 a. m.	9	130	103	15.41	8.28	7.13	41.05	48.18	140	108	79.2	1111	123	8
30 minutes after exposing aorta ..... 12: 30 a. m.	9	150	104	14.13	3.95	10.18	32.21	40.52	138	108	104.4	1026	114	6.8
35 minutes after ligating aorta	9	160	105	14.0	1.38	12.62	30	34.18	132	14	104.4	827	92	5

Protocol: 9/8/26, 10: 45 a. m., control study after 1 grain of morphine. 10 a. m., under small amount of ether anesthesia the aorta was exposed and a ligature placed around it which was not tied. 11: 50 a. m., determinations twenty minutes after placing the ligature. 11: 55 a. m., aorta occluded by ligature. 12: 30 a. m., study thirty-five minutes after occluding the aorta.

TABLE 7.—*Effect on the Cardiac Output and Blood Pressure of (1) Ligation of the Aorta, and (2) Removal of Ligature from the Aorta*

Date	Weight, Kg.	Pulse Rate, per Minute	Temperature, F.	Arterial O_2, per Cent by Volume	Venous O_2, per Cent by Volume	Arterial Venous Difference, per Cent by Volume	Arterial CO_2, per Cent by Volume	Venous CO_2, per Cent by Volume	Mean Carotid Pressure	Mean Femoral Pressure	O_2 Consumption, Cc. per Minute	Cardiac Output, per Minute, Cc.	Output per Kg., per Minute, Cc.	Output per Beat, Cc.
11/5/26														
2 p. m.; control study	14	54	100.6	12.48	7.56	4.92	45.58	48.47	100	94	145.8	2903	212	55
4:15 p. m.; 30 minutes after occluding aorta	14	140	98.8	11.04	4.32	6.72	45.60	48.60	112	20	145.8	2170	155	16
4:50 p. m.; 30 minutes after removing ligature	14	165	99.4	10.68	4.32	6.36	46.27	48.06	106	80	144	2264	162	14
5:30 p. m.; 70 minutes after removing ligature	14	150	99.6	9.96	4.56	5.40	44.62	47.37	86	70	156.6	2900	207	19
7 p. m.; 1 hour after religating aorta	14	...	.....	.....	3.24	....	.....	45.72	...	..	.....	....	...	..

Protocol: 11/5/26, 1:15 p. m., 1 grain of morphine. 2 p. m., control study. 3:45 p. m., terminal aorta ligated. 4:15 p. m., determinations. 4:20 p. m., ligature on aorta removed. 4:50 p. m., determinations. 5:30 p. m., determinations with ligature removed. 6:00 p. m., aorta occluded again. 7 p. m., sample of venous blood taken, animal died as a result of the needle puncture in obtaining arterial blood.

occlusion of the aorta, this increase is probably due to the administration of ether necessary for operative procedure. In all experiments in which the cardiac output of the animals was followed for a period of several days, it was found to increase after two or three days to an amount

equal or slightly above that found before the occlusion of the aorta. This return of the cardiac output to normal seemed to be definitely associated with the improvement in the function of the animal's posterior extremities. In most of the experiments, at the end of the second or third day, the cardiac output was increased slightly above that

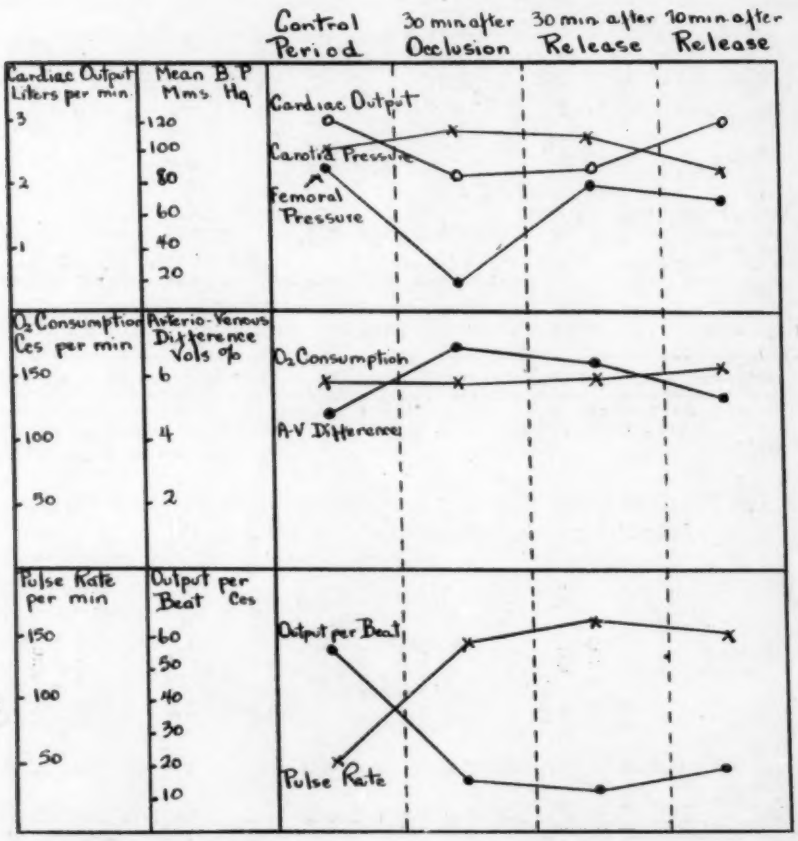

Chart 1.—A typical experiment in which the blood pressure and cardiac output were determined simultaneously during four periods, as follows: (1) control period, (2) thirty minutes after ligating the aorta, (3) thirty minutes after releasing the occlusion, and (4) seventy minutes after releasing the occlusion. It is to be noted that the carotid blood pressure is affected little by ligating the aorta, while the cardiac output decreases and rises again when the occlusion is removed. It is also seen that the changes in cardiac output are due mainly to alterations in the arteriovenous difference and not to gross changes in the consumption of oxygen.

found in the control period, but this increase was of short duration in all experiments except one (table 15). This one animal was a

female, and Marshall [6] has shown that the cardiac output is more variable in female than in male dogs.

In one experiment, the animal developed gangrene of the posterior extremities, and the cardiac output remained approximately 30 per cent less than that found before the occlusion of the aorta (table 8).

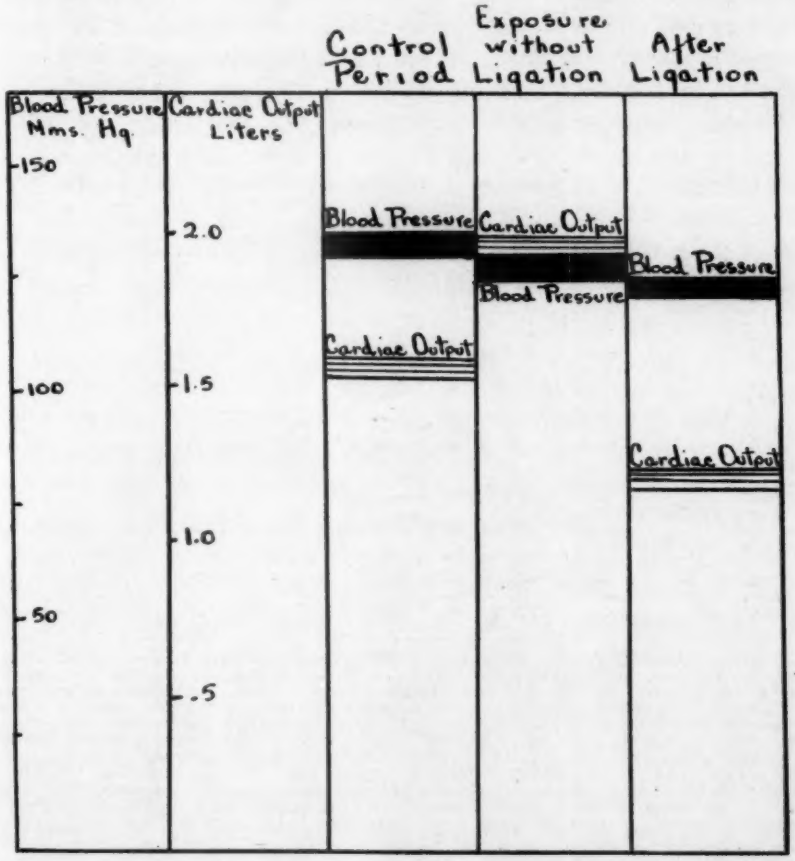

Chart 2.—The average of four experiments in which the cardiac output and blood pressure were determined simultaneously during the three periods: (1) control, (2) after exposing the aorta without occluding it, and (3) after occluding the aorta. It is to be noted that the blood pressure remained almost constant while the cardiac output fluctuated.

Autopsy of this animal failed to demonstrate any other cause for death than gangrene of the extremities.

The average decrease in the cardiac output twenty-four hours after occluding the abdominal aorta was found to be 23 per cent.

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6. Marshall, E. K.: Am. J. Physiol. **77**:459, 1926.

The rate of the consumption of oxygen usually remained about the same after occlusion of the aorta as in the control period. The decrease in cardiac output was, therefore, manifest for the most part by an increased difference between the oxygen contents of the samples of arterial and venous blood. The arterial oxygen content was found unchanged or slightly higher after the occlusion of the aorta. The arteriovenous difference was usually changed by variation in the oxygen content of the venous blood. There was a slight increase in the oxygen capacity in those experiments in which this was determined. The pulse rate increased in varying degrees.

TABLE 8.—*Effect of the Ligation of the Abdominal Aorta on the Cardiac Output*

Date	Weight, Kg.	Pulse Rate, per Minute	Temperature, F.	Arterial O_2, per Cent by Volume	Venous O_2, per Cent by Volume	Arterial Venous Difference, per Cent by Volume	Arterial CO_2, per Cent by Volume	Venous CO_2, per Cent by Volume	O_2 Consumption, Cc. per Minute	Cardiac Output, per Minute, Cc.	Output per Kg., per Minute, Cc.	Output per Beat, Cc.
9/30/26 Control study; no morphine.	8.9	120	102	14.84	9.65	5.19	33.72	37.45	102	1965	222	16
10/2/26 Control study; no morphine.	9.2	115	102.6	15.08	9.60	5.48	39.94	45.33	113.0	2062	224	18
10/5/26 Control study; no morphine.	9.0	115	102	15.08	9.41	5.67	39.11	45.74	112.5	1984	220	17
10/6/26 24 hours postoperative; no morphine	8.7	180	102.2	14.84	10.02	4.82	37.31	39.66	94.5	1961	225	11
10/7/26 2 days postoperative; no morphine	8.5	180	103.2	12.77	6.94	5.83	40.06	42.17	90.0	1544	182	9
10/10/26 No morphine	7.7	150	104	9.93	2.91	7.02	35.61	37.42	101	1439	187	9

Protocol: Healthy young male dog. 9/30/26, 10/2/26 and 10/5/26, control studies without morphine. 10/5/26, aorta ligated twice above trifurcation and cut between ligatures, the lowest lumbar artery on the right side was also ligated. 10/6/26, animal able to walk using left foot, but drags the right one. Studies made twenty-four hours after operation without morphine. 10/7/26, twenty-four hours after ligation, determinations without morphine. Animal still unable to use his right leg in walking. The right leg is definitely cooler than the left. 10/10/26, dog does not look well, but is able to walk. Superficial infection of incision. Discharge from nose. Determinations. 10/12/26, animal died. Nothing found at autopsy to account for death. No pneumonia. No apparent enlargement of heart. No thrombi in heart. Ligature on aorta in place, no thrombosis. No peritonitis. No gangrene of extremities. Superficial infection of incision.

(b) The Effect on the Blood Pressure of Occlusion of the Abdominal Aorta.—Fourteen experiments were performed in which the blood pressure in the carotid and femoral arteries was determined before, during and after the occlusion of the abdominal aorta. In twelve of these, the blood pressure was recorded continuously throughout the experiment and the animal was killed at its termination. In the remaining two experiments, the aorta was completely occluded and the animals were allowed to recover. The general condition of the two animals was observed from time to time, and studies of the determinations of the blood pressure were carried out after five and eight months.

In twelve experiments, the duration of the study varied in time from less than an hour to more than ten hours. The blood pressure

was found to remain relatively constant during the control period of the study. It became slightly elevated during the administration of a small amount of ether preliminary to operation. A temporary fall in blood pressure resulted from opening the abdomen and exposing the aorta. Sufficient time was allowed to elapse for the pressure to reach a constant level and then the aorta was occluded. This pressure was usually slightly lower than that which was present at the beginning of the experiment. Immediately following occlusion of the aorta, there was an average rise of 10 mm. of mercury in the carotid pressure in the nine experiments in which the mean pressure was recorded. Simultaneously, with the occlusion of the aorta, there was always a momentary stiffening of the posterior extremities. It is possible that this caused the rise in pressure. The elevation in the carotid pressure did not persist longer than two minutes in any instance. This preliminary rise in the carotid pressure was followed by a momentary decline, which in turn was followed by a slight elevation over a period of from five to ten minutes. The level reached at this time was usually maintained for several hours. In no instance was a marked subsequent rise encountered. These points are illustrated in chart 3.

Immediately after occlusion of the aorta, there was an abrupt fall in the pressure in the femoral artery. The rate of rise in the femoral pressure following the sudden decrease was variable. The greatest increase which was encountered was an elevation of 16 mm. of mercury forty minutes after the occlusion had been produced, and it remained at this level for several hours. The results of these experiments are recorded in table 17 and represented graphically in chart 4.

In the remaining two experiments, the remote effects of occlusion of the aorta on the blood pressure were studied. Recovery from the operation, in which the abdominal aorta was occluded, was uneventful in each instance except for weakness and stiffness of the posterior extremities which persisted for two and five days respectively. Both of these animals were able to use their legs in walking shortly after regaining consciousness from the anesthetic. A palpable femoral pulse was first noted in one animal four months after the ligation of the aorta. One month later, the mean carotid pressure was 150 mm. of mercury, and the mean femoral pressure 114 mm. of mercury. In the other animal, a palpable femoral pulse was detected three months after the operation. Five months later, the mean carotid pressure was 118 mm. of mercury, and the mean femoral pressure was 108 mm. of mercury. At autopsy, the terminal aorta was found to be occluded completely in both of these animals. There was no evidence of hypertrophy of the heart.

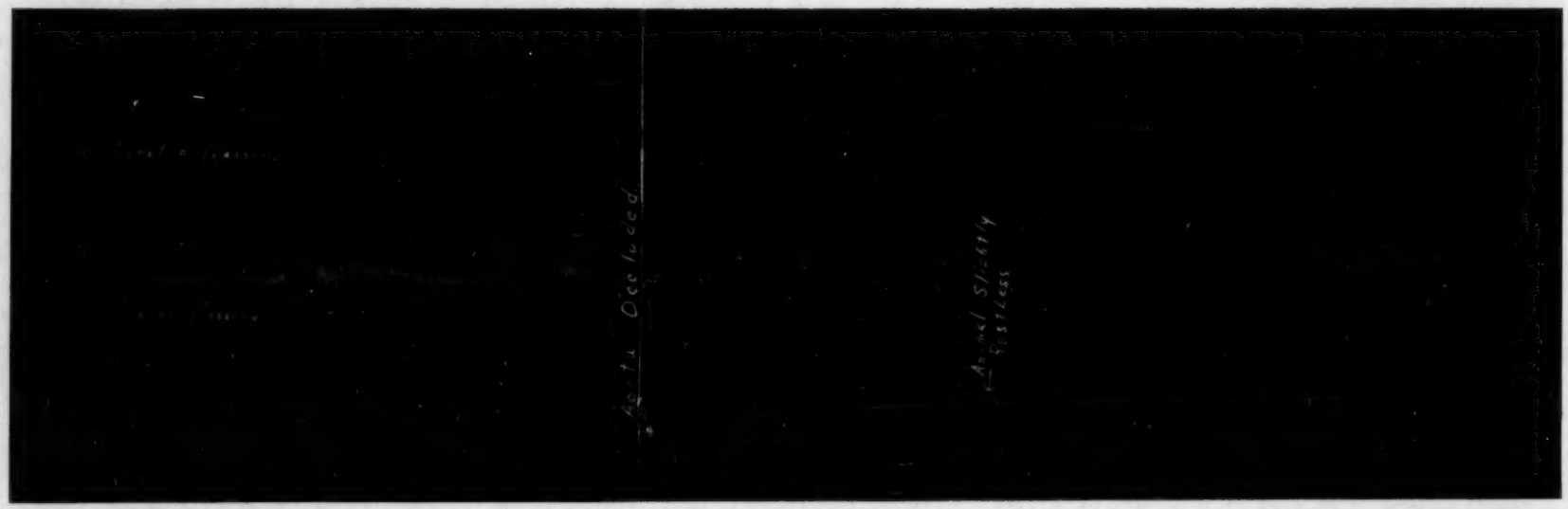

Chart 3.—A typical tracing of the blood pressures in the carotid and femoral arteries before and after occlusion of the abdominal aorta. Time was recorded in minutes. It will be noted that the carotid pressure throughout is surprisingly uniform. There is shown a slight rise immediately following occlusion of the aorta, which persists but a minute. The femoral pressure shows some slow gradual rise during the forty minutes after occlusion of the aorta. This experiment was conducted over a period of ten hours. During the remainder of the time, the carotid and femoral pressure were very constant and changed little from the level shown in the portion of the record here produced.

(c) The Effects of Occlusion of the Abdominal Aorta on the Distribution of the Blood Volume.—The method of study of the effects of occlusion of the abdominal aorta on the distribution of the blood volume was as follows: A dog was anesthetized with ether and securely fixed to a board which was balanced in the same manner as the platform balance. A pointer attached to one end of the board was adjusted to trace a line on a revolving kymograph. With this adjustment the respiratory movements caused the point to trace a curve on the kymograph paper similar to that obtained by the usual method of obtaining respiratory tracings. A clamp was then adjusted so that the abdominal aorta could be obstructed and released without disturbing the balance of the animal board. It was found that alternate obstruction and release of

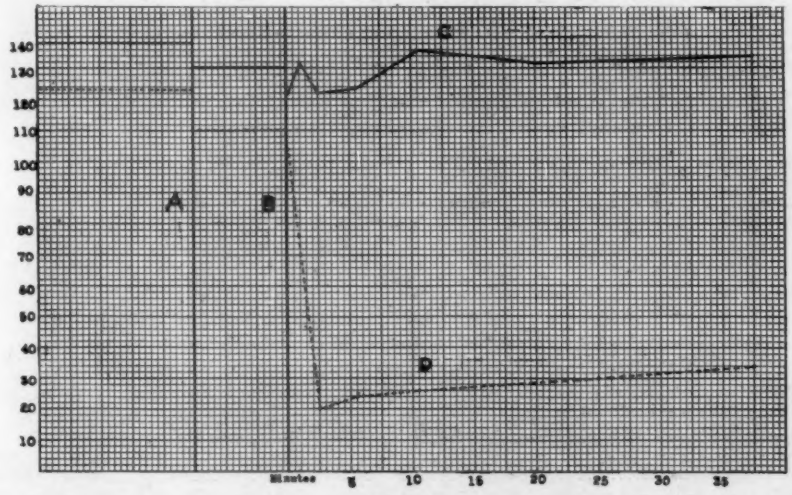

Chart 4.—The average height of blood pressure in the carotid and femoral arteries at various times during observations on the nine experiments in which the mean pressure was measured. In the control part of the experiment and after exposure of the aorta, the pressures were allowed to reach constant levels. These constant levels were measured, and their average height is shown at the left hand side of the figure. In the blood pressure tracings from these nine experiments the height of the two pressures was measured immediately after the occlusion of the aorta, also two, five, ten, twenty and forty minutes after occlusion. The average pressure thus measured is plotted accurately as to time and pressure in millimeters of mercury.

obstruction of the abdominal aorta resulted in immediate changes in the balance of the animal. Immediately after obstruction of the aorta, the end of the board toward the posterior aspect of the animal would rise. This relative change in the weights of the posterior and anterior aspects of the animal's body persisted for the entire duration of each observation. It is obvious that the nature of the conditions made it impossible

TABLE 9.—*Effect of the Ligation of the Abdominal Aorta on the Cardiac Output*

Date	Weight, Kg.	Pulse Rate, per Minute	Temperature, F.	Arterial O_2, per Cent by Volume	Venous O_2, per Cent by Volume	Arterial Venous Difference, per Cent by Volume	Arterial CO_2, per Cent by Volume	Venous CO_2, per Cent by Volume	O_2 Consumption, Cc. per Minute	Cardiac Output, per Minute, Cc.	Output per Kg., per Minute, Cc.	Output per Beat, Cc.
9/11/26												
Control study; no morphine..	9	75	100.6	16.10	8.28	7.82	32.72	38.49	88.5	1182	131	15
9/13/26												
Control study; ¾ grain morphine	9	56	100.8	16.16	7.89	8.27	40.26	45.32	88.2	1066	118	19
9/17/26												
Control study; ¾ grain morphine	8.6	70	102	15.57	8.0	7.57	42.0	43.73	81	1070	124	15
9/20/26												
3 days after ligation; ¾ grain morphine	8.1	56	104	12.38	6.19	6.19	47.05	52.65	76.8	1241	153	22
9/24/26												
¾ grain morphine; gangrene both feet	7.7	125	104	9.94	3.61	6.33	47.45	52.59	81	1279	166	10

Protocol: 9/11/26, 9/13/26 and 9/17/26, control studies with and without morphine. 9/17/26, terminal aorta ligated twice and divided between ligatures. 9/20/26, dog able to walk. Looks fairly well. 9/24/26, animal has gangrene of both feet of the posterior extremities. He was killed after the determination. The gangrene was slightly more marked in the left foot. Superficial gangrene extended up into the thigh. That in the skin and subcutaneous tissues extended to a higher level than that in the muscle. There was no thrombus in the proximal end of the aorta, but there was a small one in the right iliac vessel. There was a mural antemortem thrombus on the wall of the left ventricle. Observer was unable to tell whether or not the divisions of the terminal aorta had been occluded by the ligature.

TABLE 10.—*Effect of the Ligation of the Abdominal Aorta at the Trifurcation*

Date	Weight, Kg.	Pulse Rate, per Minute	Temperature, F.	Arterial O_2, per Cent by Volume	Venous O_2, per Cent by Volume	Arterial Venous Difference, per Cent by Volume	Oxygen Capacity, per Cent by Volume	Saturation, per Cent	O_2 Consumption, Cc. per Minute	Cardiac Output, per Minute, Cc.	Output per Kg., per Minute, Cc.	Output per Beat, Cc.
1/6/26												
Control study, 1 grain morphine	8.9	56	99	16.14	10.53	5.61	16.35	98.7	77.36	1379	155	24.6
1/8/26												
24 hours after operation, 1 grain morphine.....	8.64	230	100.4	18.8	10.36	7.44	.....	....	77.36	1039	120	4.4.

Protocol: 1/6/26, control study, 1 grain of morphine. 1/7/26, aorta ligated 5 cm. above trifurcation, two lower lumbar arteries also being ligated. Dog did not give appearance of being in shock. 1/8/26, determinations made after 1 grain of morphine. Unable to walk. Condition seemed good. 1/9/26, animal died. No peritonitis, small amount of consolidation of lungs, ligatures on aorta in place.

TABLE 11.—*Effect of the Ligation of the Abdominal Aorta on the Cardiac Output*

Date	Weight, Kg.	Pulse Rate, per Minute	Temperature, F.	Arterial O_2, per Cent by Volume	Venous O_2, per Cent by Volume	Arterial Venous Difference, per Cent by Volume	Arterial CO_2, per Cent by Volume	Venous CO_2, per Cent by Volume	O_2 Consumption, Cc. per Minute	Cardiac Output, per Minute Cc.	Output per Kg., per Minute Cc.	Output, per Beat Cc.
9/27/26												
Control study, 1 grain morphine	14.5	60	100.4	17.61	12.67	4.94	53.5	55.28	105.4	2133	147	36
9/28/26												
24 hours after ligation.....	14.2	175	100	19.30	13.27	6.03	36.9	43.12	110.6	1834	129	10

Protocol: 9/27/26, control study after 1 grain of morphine. The terminal aorta was ligated twice and divided between the ligatures. 9/28/26, study after ¾ grain of morphine. Dog looked badly, not able to walk. Some swelling of the posterior extremities. 9/28/26, animal died. There was an enormous amount of swelling of the posterior extremities which extended up into the lower abdominal wall. There was no thrombus in the proximal aorta nor in the vessels below the trifurcation. No thrombus in the heart.

TABLE 12.—*Effect of the Ligation of the Abdominal Aorta*

Date	Weight, Kg.	Pulse Rate, per Minute	Temperature, F.	Arterial O_2, per Cent by Volume	Venous O_2, per Cent by Volume	Arterial Venous Difference, per Cent by Volume	Oxygen Capacity, per Cent by Volume	Arterial CO_2, per Cent by Volume	Venous CO_2, per Cent by Volume	O_2 Consumption, Cc. per Minute	Cardiac Output, per Minute Cc.	Output per Kg., per Minute, Cc.	Output per Beat, Cc.
3/15/26													
4:30 p. m. Control study, 1 grain morphine	10.3	60	100	14.33	8.22	6.21	.....	53.55	57.82	101.45	1634	158.6	27
3/15/26													
10 p. m. Control study, 1 grain morphine	10.3	60	100	15.68	9.96	5.72	.....	44.75	48.95	94.0	1644	159.6	27
3/16/26													
Control study, no morphine	10.3	150	103	13.74	7.48	6.26	.....	41.53	45.15	99.8	1504	154.7	10.6
3/29/26													
Control study, ½ grain morphine	10.0	54	99	15.53	9.01	6.52	.....	39.07	45.89	102.5	1572	157.2	29
4/1/26													
20 hours following ligation; no morphine	9.1	200	102	12.9	6.79	6.11	.....	40.01	43.92	88.56	1449	159	7.1
4/2/26													
44 hours after operation; ½ grain morphine	9.1	180	102	10.84	5.21	5.63	11.69 98%	.....	.....	92.25	1639	180	9.1
			4/3/26. Temperature 104										
4/4/26													
Infection of incision; no morphine	9.4	180	103.8	9.02	3.88	5.14	.....	44.17	52.96	129.15	2513	267	14
4/6/26													
No morphine	9.6	180 (?)	104	9.64	3.06	6.58	9.80 98.4%	45.21	51.65	121.77	1851	193	10.3
4/22/26													
No morphine	9.8	108	102.4	12.26	6.13	6.13	12.93 94.8%	42.91	44.76	103.3	1685	172	15.6

Protocol: Control studies made on 3/15/26, 3/16/26 and 3/29/26. 3/31/26, aorta ligated. 4/1/26, animal able to walk, drags back legs slightly. Determinations without morphine. 4/3/26, slight infection of incision, dog does not look well. 4/10/26, incision healed. 4/22/26, dog looks well, incision completely healed. 4/28/26, dog killed by hemopericardium. Autopsy revealed no peritonitis, ligatures on aorta in place. X-ray examination showed very good collateral circulation.

TABLE 13.—*Effect of the Ligation of the Abdominal Aorta*

Date	Weight, Kg.	Pulse Rate, per Minute	Temperature, F.	Arterial O_2, per Cent by Volume	Venous O_2, per Cent by Volume	Arterial Venous Difference, per Cent by Volume	Oxygen Capacity, per Cent by Volume	Saturation, per Cent	O_2 Consumption, Cc. per Minute	Cardiac Output, per Minute, Cc.	Output per Kg., per Minute, Cc.	Output per Beat, Cc.
5:45 p. m. Control study	11	90	99	18.47	10.92	7.55	18.96	97	104.8	1388	126	15.4
8:40 p. m.; 2 hours after ligation	11	160	96	18.1	7.96	10.14	18.65	92	108	1065	97	6.7
10:40 p. m.; 4 hours after ligation	11	200	96	18.67	8.77	9.90	19.0	98	108	1071	97.4	5.4

Protocol: 4:00 p. m., 1 grain of morphine. Tracheotomy tube placed in. 5:45 p. m., control study. 6:30 p. m., aorta ligated under local anesthesia, animal fairly quiet during procedure. 8:40 p. m., second determinations, animal slightly restless. 10:40 p. m., third determinations. Animal killed after determinations completed. Examination showed ligature in place, producing complete occlusion of the aorta.

TABLE 14.—*Effect of the Ligation of the Abdominal Aorta*

Date	Weight, Kg.	Pulse Rate, per Minute	Temperature, F.	Arterial O_2, per Cent by Volume	Venous O_2, per Cent by Volume	Arterial Venous Difference, per Cent by Volume	Oxygen Capacity, per Cent by Volume	Saturation, per Cent	O_2 Consumption, Cc. per Minute	p_H	Cardiac Output, per Minute, Cc.	Output per Kg., per Minute, Cc.	Output per Beat, Cc.
12/9/25													
Preoperative; 1 grain morphine	9.55	60	100.3	16.60	10.82	5.78	18.1	91.7	77.7	7.32	1344	141	22.4
12/9/25													
4½ hours after operation	9.55	49	96	18.38	11.71	6.68	19.04	96.6	80.72	7.42	1210	127	24.7
12/10/25													
20 hours after operation	9.3	138	101.6	18.07	9.93	8.14	19.0	95.1	80.36	7.49	988	100.6	7.2
12/11/25	9.0	100	102.6	16.28	10.94	5.34	16.5	98.7	86.0	....	1610	179	10.1
12/13/25	8.9	135	102.7	15.34	10.71	4.63	15.54	98.7	91.4	....	1978	222	14.6
12/19/25	8.18	180	104	12.91	7.62	5.29	13.78	93.7	76.8	....	1450	177	8.1

Protocol: 12/9/25, control study followed by ligation of aorta; aorta divided between two ligatures. 12/10/25, studies without morphine. Dog looks well, but cannot walk. 12/11/25, animal able to walk, looks well. 12/12/25, looks well, infection of incision line. 12/15/25, increase in amount of infection of incision, abdomen soft on palpation. 12/19/25, infection of incision about the same. Animal killed, no general peritonitis. Ligatures on aorta in place. Animal injected with bismuth sulphate, good collateral circulation shown by x-ray examination.

TABLE 15.—*Effect of the Ligation of the Abdominal Aorta on the Cardiac Output*

Date	Weight, Kg.	Pulse Rate, per Minute	Temperature, F.	Arterial O_2, per Cent by Volume	Venous O_2, per Cent by Volume	Arterial Venous Difference, per Cent by Volume	Arterial CO_2, per Cent by Volume	Venous CO_2, per Cent by Volume	O_2 Consumption, Cc. per Minute	Cardiac Output, per Minute, Cc.	Output per Kg., per Minute, Cc.	Output per Beat, Cc.
8/23/26												
Control study; 1 grain morphine	16.2	42	100	21.32	16.1	5.22	.....	.....	126	2114	131	50
8/26/26												
1 grain morphine.....	15.9	44	98.6	18.0	13.73	4.27	.....	.....	109.5	2564	161	58
9/2/26												
1 grain morphine.....	14.7	60	101.4	17.92	12.29	5.63	43.33	47.17	126	2238	152	37
9/10/26												
1½ grains morphine.....	14.9	54	101.8	16.46	12.31	4.15	40.47	44.76	126	3036	204	56
9/20/26												
¾ grain morphine.....	15	56	101.6	18.99	14.27	4.72	42.06	49.32	166	3517	234	63
10/6/26												
5/4 grains morphine.....	15	54	100.8	17.81	13.0	4.81	53.51	58.56	122.4	2524	168	47
10/8/23												
5/4 grains morphine.....	15	56	100.4	17.55	12.59	4.96	56.89	62.17	120	2419	161	43

Protocol: 8/23/26, healthy female dog. Control study after 1 grain of morphine. The aorta was ligated twice just above the trifurcation and divided between the ligatures after the control determinations. 8/26/26, looks well. Quiet during determinations. 9/2/26, animal quiet during determinations. 9/10/26, animal fairly quiet during determinations. 9/20/26, animal restless during determinations. 10/6/26, 5/4 grains morphine. Animal quiet during determinations. Looks well. 10/8/26, 5/4 grains morphine. Animal quiet during determinations. Femoral arterial pulsations felt. O_2 content femoral artery was 17.19; CO_2 content 54.94.

to observe the change for a long period since any movement in the animal's body operated to change the condition of balance.

The result of the release of the obstruction of the aorta was particularly interesting. If the animal was brought into a state of

TABLE 16.—*Effect of the Ligation of the Abdominal Aorta at the Trifurcation*

Date	Weight, Kg.	Pulse Rate, per Minute	Temperature, F.	Arterial O_2, per Cent by Volume	Venous O_2, per Cent by Volume	Arterial Venous Difference, per Cent by Volume	Oxygen Capacity, per Cent by Volume	Saturation, per Cent	O_2 Consumption, Cc., per Minute	Cardiac Output per Minute, Cc.	Output per Kg., per Minute, Cc.	Output, per Beat, Cc.
1/14/26												
Preoperative control study..	10.2	56	.....	19.03	15.03	4.0	20.3	93.7	80.9	2022	198	36
1/15/26												
9 hours postoperative.....	10	76	.....	22.3	17.07	5.23	23.53	94.8	77.22	1476	147.6	19
1/16/26	10	92	100.8	19.2	15.2	4	20.5	93.7	80.9	2022	202.2	22

Protocol: 1/14/26, control study, 1 grain morphine. 1/15/26, aorta ligated just above the trifurcation. Animal able to walk three hours following completion of the operation. X-ray examination at this time showed normal heart and lungs. Studies made nine hours following completion of the operation ¾ grain of morphine used. 1/16/26, ¾ grain, third series of observations made. 1/18/26, evidence of distemper. 1/21/26, animal died. X-ray examination previous to death showed pneumonia on left side and a heart of normal size. Autopsy revealed extensive pneumonia. Ligatures on aorta in place.

TABLE 17.—*Effect on (1) the Mean Carotid Blood Pressure and (2) the Mean Femoral Blood Pressure of Ligation of the Abdominal Aorta* *

Experiment Number	Date	Control Pressure		Immediately after Exposure		Immediately before Occlusion		Immediately after Occlusion		2 Minutes after Occlusion		5 Minutes after Occlusion		10 Minutes after Occlusion		20 Minutes after Occlusion		40 Minutes after Occlusion	
		Carotid	Femoral	Carotid	Femoral	Carotid	Femoral	Carotid	Femoral	Carotid	Femoral	Carotid	Femoral	Carotid	Femoral	Carotid	Femoral	Carotid	Femoral
41	10/ 5/26	86	88	65	68	60	68	74	34	72	9	74	9	...	...	...	...	...	...
39	9/21/26	152	114	174	120	152	114	178	82	154	18	174	32	...	...	...	...	...	...
42	11/ 6/26	...	...	122	120	94	90	96	38	74	36	50	34	...	...	...	...	...	...
46	11/ 3/26	146	138	134	118	142	128	...	...	142	...	148	...	136	20	...	...	...	...
37	9/ 8/26	144	122	164	122	114	76	132	22	128	12	128	12	118	12	130	12	...	...
44	10/21/26	162	154	142	130	148	142	154	100	140	46	148	42	158	42	...	...	...	...
36	9/ 3/26	136	126	118	90	148	112	154	20	142	22	140	20	138	32	134	34	134	34
45	10/ 2/26	150	130	136	120	130	116	138	34	126	16	130	20	...	...	...	...	...	...
47	11/ 5/26	...	...	102	104	110	94	134	20	110	12	114	16	...	...	...	...	...	...
	Average...	139	124	130	110	122	104	132	43	121	21	123	24	137	26	132	28	134	34

* This table shows the actual pressures in millimeters of mercury in the carotid and femoral arteries in nine experiments in which the mean pressure was measured. The measurements were taken during the control portion of the experiment, immediately after exposure of the aorta, immediately before occlusion of the aorta, immediately after occlusion of the aorta, and two, five, ten, twenty and forty minutes after its occlusion. The averages of these are given below. These are the figures plotted in figure 4.

balance and a clamp applied to the aorta, the posterior aspect of the animal would become relatively lighter, and the writing point at the foot of the balance board would make a tracing at a higher level on the kymograph paper. If the clamp obstructing the aorta was then allowed to remain in a position for a period of five or ten minutes,

the curve traced by the writing point assumed an almost constant level. If the clamp was then removed from the aorta, the weight of the posterior aspect of the animal's body became immediately greater. The amount of relative increase in weight of the posterior aspect of the animal's body was such that the writing point descended on the kymograph paper to a level lower than before the aorta was obstructed, and there was a visible hyperemia of the skin of the posterior extremities.

From the results obtained from these relatively crude experiments, it was obvious that occlusion of the abdominal aorta resulted in an immediate shifting of the blood volume from the vessels on the distal aspect of the obstruction to those proximal to the point of obstruction. This is in contrast to the generally accepted opinion that slowing of the circulation is associated with an accumulation of blood in the peripheral vessels and fluid in the tissues. It is, of course, obvious that the results obtained in these experiments are only indicative of what happens immediately after the occlusion of an artery. The relationship between edema and arterial obstruction has already been discussed in a previous publication.[7] It might be that the increased blood volume in the anterior part of the animal's body was contained in a dilated heart or congested pulmonary circulation, but it would seem as if such a condition would be associated with increased blood pressure in the aorta. Such is not the case. The possible importance of the changes in the distribution of blood volume immediately following occlusion of the abdominal aorta as a factor influencing the changes in the blood pressure will be discussed later.

COMMENT

The results of the experiments described in this paper bear particularly on the study of the effects on the heart of occlusion of the abdominal aorta. The experiments show that occlusion of the abdominal aorta results in the following changes:

1. The cardiac output is decreased.
2. There is little, if any, change in the blood pressure in the artery proximal to the occlusion.
3. Immediately following the occlusion there is a transfer of the blood volume from the distal to the proximal aspect of the obstruction.

The amount of work which is done by the heart is expressed by the following formula: $W = Mp$ plus $\frac{MV^2}{2g}$ in which W is the work

7. Brooks, Barney: Pathologic Changes in Muscle as a Result of Disturbances of Circulation: An Experimental Study of Volkmann's Ischemic Paralysis, Arch. Surg. **5**:188 (July) 1922.

of the heart, M is the mass of blood put out in a unit of time, P is the average arterial pressure and V is the velocity of the blood at the base of the aorta during ventricular expulsion. From a study of the relationship existing between the various factors of this formula, it is clear that the substitution in it of the values resulting from obstruction of the aorta would not increase the value of the factor W. The fact that blood pressure in the base of the aorta is so little altered by the relatively great changes in the conditions of the peripheral circulation which must follow the occlusion of so large a vessel, as the abdominal aorta, is evidence of the importance of the vagopressor reflex which operates to keep the arterial blood pressure constant in the presence of alterations in venous pressure and cardiac output.

The fact that the conclusions reached in this study are contradictory to those of Katzenstein deserves a word of comment. From a study of the experiments described in this paper and those described by Katzenstein, it is clear that the effects on the blood pressure observed immediately after obstruction of the aorta are not essentially different. In Katzenstein's experiments, the most marked elevations of blood pressure observed and attributed to the effect of ligation of the aorta were in instances in which the intra-arterial tension was determined before the aorta was ligated, and then again after periods of from three days to four weeks.

In the experiments described in this paper, great care was taken to observe the effects of occlusion of the abdominal aorta under conditions of the circulation which were as nearly normal as possible. From a study of the protocols of the experiments described by Katzenstein, it appears that in at least some of his experiments the blood pressure was abnormally low at the time the aorta was obstructed. Most of his experiments were conducted on animals anesthetized with chloroform. This anesthetic produces marked effects on the blood pressure. Some of Katzenstein's experiments were performed on animals paralyzed with curare. Although this drug apparently does not have any effect on the blood pressure, it is probable that the experimental animal under the influence of curare is in a condition in which other factors produced changes in blood pressure which would not occur if this drug had not been administered.

In the experiments conducted for this study in which the experimental animals were examined after relatively long periods had elapsed since the occlusion of the aorta, no evidence was found of hypertrophy of the heart.

It was thought that the shifting of the blood volume in the animal's body might account for some of the changes in the blood pressure observed to follow ligation of the abdominal aorta. For example, it

seems possible that if the experimental animal was in a condition in which the blood pressure was low and the functioning blood volume was decreased, then obstruction of the aorta and the consequent shifting of the blood volume from the distal to the proximal aspect of the obstruction would operate to increase the blood pressure in the base of the aorta. In order to test this, some additional experiments were performed in which the effect of occlusion of the aorta in animals with low blood pressure was studied. It was found that if the blood pressure in the carotid artery was low, then occlusion of the aorta resulted in a small temporary rise of blood pressure which was apparently not different from that observed in animals in which the blood pressure was normal. If the aorta was obstructed in an animal in which the blood pressure was low and if sufficient time was allowed to elapse for the disappearance of the temporary rise in the carotid pressure, then release of the obstruction of the aorta resulted in a marked sudden fall in the carotid pressure which slowly returned to the former level. The form of the blood pressure curve, immediately after the obstruction and release of obstruction of the abdominal aorta, is such as to suggest that the changes in blood pressure on the proximal aspect of the ligature is due to the changes of the distribution of the blood volume.

OSSIFICATION AFTER FRACTURE

AN EXPERIMENTAL STUDY *

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In 1926, one of us (I. S. R.) with Jonas [1] studied the serum calcium and inorganic phosphorus in a series of patients with fractures at diversified sites. From this study we were doubtful as to whether the serum calcium and inorganic phosphorus content in clinical cases could be used as a prognostic index for union or nonunion in the majority of instances.

In 1924, Shipley [2] investigated conditions under which calcification occurred in vitro. He found that in slabs of completely rachitic bones, incubated in normal serum, calcification occurred promptly, whereas sections of the same bone in rachitic serum failed to calcify. In 1926, Shipley, Kramer and Howland [3] repeated and confirmed Shipley's results, and showed, also, that calcification occurred promptly in slabs of rachitic bone incubated in solutions of inorganic calcium and phosphorus in concentrations similar to those of normal serum. It was their opinion that failure to produce calcification in vivo was dependent on an insufficient concentration of calcium and inorganic phosphorus in the fluids around the growing bone. Remarkable as it may seem, these investigators found that calcification in vitro occurred within from sixteen to twenty-four hours when the concentrations of inorganic calcium and phosphorus were 7 and 5 mg., respectively, per hundred cubic centimeters as well as when they were 10 and 3.5 mg., respectively.

In 1922, Howland and Kramer [4] published the results of a study of the calcium and phosphorus of the serum in children with rickets and in those with rickets complicated by tetany. They believed that the determining factor in the calcification of bone in these cases was the presence of calcium and phosphorus in such amounts that the product

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* From the Laboratory of Surgical Research and the William Pepper Laboratory, University of Pennsylvania.

1. Ravdin, I. S., and Jonas, L.: Ann. Surg. **34**:37, 1926.

2. Shipley, P. G.: Bull. Johns Hopkins Hosp. **35**:304, 1924.

3. Shipley, P. G.; Kramer, Benjamin, and Howland, John: Biochem. J. **20**: 379, 1926.

4. Howland, John, and Kramer, Benjamin: Tr. Am. Pediat. Soc. **34**:204, 1922.

of their concentrations, expressed in milligrams per hundred cubic centimeters of serum, equalled a certain minimal figure, which lay roughly between 30 and 40.

In 1924, Petersen [5] studied a series of clinical cases of nonunion, and a series of dogs after experimental fracture. He believed that the underlying basis of many cases of nonunion was made manifest in a deficiency in either a subnormal calcium or an inorganic phosphorus content of the serum. He used the calcium and phosphorus product advocated by Howland and Kramer to show this deficiency. He found the optimum product for healing to be between 35 and 40, while products less than 30 were the rule in patients with nonunion.

Since our work was carried out on patients suffering with fractures at diversified sites, it seemed necessary to obtain for study a series of cases in which the fractures occurred at the same site and were produced in the same way in persons of approximately the same age. It was necessary, therefore, to utilize an experimental animal for this work.

We wished to ascertain: (1) whether ossification would occur in a shorter period of time in the normal animal after the administration of parathyroid extract-Collip, which increases calcium retention in the blood, than in the normal control animal; (2) whether cod liver oil alone, which increases phosphorus and sometimes calcium retention in the rachitic animal, would have any beneficial effect on ossification in the normal animal; and (3) whether union would occur after a considerable fall in the serum calcium, as is found after thyroparathyroidectomy.

EXPERIMENTAL WORK

Small young dogs were used for this work. The site selected for fracture was the radius, just below the middle of the shaft. The bone was exposed and fractured with a chisel. After fracture, the wound was closed and a molded aluminum splint was applied. All operations were performed under careful aseptic technic and no infections occurred. The dogs were healthy stock animals, of about the same age, but they did not belong to the same litter. They were kept on a diet of dog biscuits and milk, and were given as much as they would eat.

Fracture was produced in: (1) normal control dogs, (2) dogs receiving 20 cc. of cod liver oil daily, (3) dogs in which the serum calcium level was raised by the administration of parathyroid extract-Collip and (4) dogs in which the serum calcium level was lowered by thyroparathyroidectomy.

The last mentioned animals were prepared for thyroparathyroidectomy by the method of Jones,[6] i. e., feeding 20 cc. of cod liver oil daily, beginning two weeks before the removal of the glands. Only one dog lived until union of the fracture was complete. This one was in excellent condition and was killed 186 days after thyroparathyroidectomy.

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5. Petersen, Henry A.: J. Bone & Joint Surg. **22**:885, 1924; Bull. Johns Hopkins Hosp. **35**:378, 1924.

6. Jones, J. H.: J. Biol. Chem. **70**:647, 1926.

Calcification was followed by x-ray pictures the tenth day after fracture and as nearly as possible every week thereafter.

The serum calcium was determined by the method of Kramer and Tisdall,[7] and the serum inorganic phosphorus by the method of Fiske and Subbarow.[8] Estimations were made every two weeks, except in the hypercalcemic and hypocalcemic dogs, on whom estimations were made more frequently in an attempt to more carefully follow the levels.

RESULTS

Table 1 gives the x-ray observations. This work was done by Dr. Henry Pancoast of the Hospital of the University of Pennsylvania.

TABLE 1.—*Report on X-Ray Observations*

Number Days After	Normal Controls		Cod Liver Oil Controls		Hypercalcemic		Hypocalcemic		
Fracture	No. 36	No. 48	No. 10	No. 22	No. 12	No. 60	No. 17	No. 27	No. 15
10	Slight periosteal reaction	No callus	.....	Very slight callus	.....	Very slight callus	Very slight callus	No evidence of callus	No callus
17	.....	No callus	Very slight callus	Considerable callus	Union	Slight periosteal callus	Slight callus	No callus	
24	More callus	Slight callus formation	Slight callus formation	.....	.....	Some increase in callus	.....	Death	
31	Union	More external callus	More callus	.....	.....	.....	Slight increase in callus	.....	Slight callus
38	.....	Considerably more callus	Union	Union with excessive external callus	.....	More callus	More callus	.....	Death
45	.....	Union	.....	.....	.....	Union	Considerable external but very little intermediate callus		
52	.....	.....	.....	.....	.....	.....	Increase in external callus		
66	.....	.....	.....	.....	.....	.....	Almost united		
71	.....	.....	.....	.....	.....	.....	Union		

The x-ray examination coincided closely with the physical examination of the extremity and at the time that the roentgen-ray picture showed union, the animal was able to walk without a limp. The number of days in this table is not absolute. Several vary as much as two or three days. In dogs 15, 22 and 36, certain plates unfortunately were lost.

Table 2 shows the calcium and phosphorus values (*a*) immediately before fracture, (*b*) immediately after fracture and (*c*) at the time of union. Column 1 shows the serum calcium content in milligrams per hundred cubic centimeters; column 2, the serum calcium content

7. Kramer, B., and Tisdall, F. F.: J. Biol. Chem. **47**:475, 1921. Tisdall, F. F.: J. Biol. Chem. **56**:439, 1923.

8. Fiske, Cyrus H., and Subbarow, Yellapragada: J. Biol. Chem. **66**:375, 1925.

in mols; column 3, the serum inorganic phosphorus in milligrams per hundred cubic centimeters; column 4, the serum inorganic phosphorus in mols; column 5 the calcium and phosphorus product, advocated by Howland and Kramer [4] and later by Petersen,[5] and column 6, the ($PO_4\equiv$) in mols (determined according to Holt, La Mer, and Chown.[9] In columns 6 and 7, we assume a p_H of 7.4. Column 7 shows the $Ca_3(PO_4)_2$ ion product and column 8, the negative logarithm of the $Ca_3(PO_4)_2$ ion product, as advocated by Holt.[10] Holt [10] concluded that

TABLE 2.—*Calcium and Phosphorus Values Immediately Before and After Fracture, and at Union*

	1	2	3	4	5	6	7	8		
Dog	Ca, Mg. per 100 Cc.	(Ca^{++}) Mols per Liter	P, Mg. per 100 Cc.	(P) Mols per Liter	Ca × P, Mg. per 100 Cc.	($PO_4\equiv$) Mols per Liter	$(Ca^{++})^3 (PO_4)^2$	−Log. Prod. (p Prod.)	Union, Days	Average
Normal Controls										
36 a.	11.6	2.89 10-3	9.9	0.93 10-3	33.6	6.60 10-9	10.70 10-25	23.97		
b.	11.4	2.85	3.5	1.13	39.9	8.12	15.56	23.81	30	
c.	11.0	2.77	3.6	1.15	39.6	8.27	14.56	23.84		37.5
48 a.	10.9	2.72	3.8	1.22	41.4	8.77	15.46	23.81		
b.	11.3	2.82	3.5	1.13	39.6	8.12	14.76	23.83	45	
c.	10.9	2.72	3.3	1.06	35.9	7.62	11.68	23.93		
Cod Liver Oil Controls										
10 a.	11.5	2.87	3.6	1.15	41.4	8.27	16.14	23.79		
b.	10.7	2.67	3.0	0.97	32.1	6.97	9.22	24.04	36	
c.	11.8	2.94	3.3	1.06	38.9	7.62	14.76	23.83		37.5
22 b.	11.7	2.92	4.7	1.51	55.0	10.86	29.39	23.53		
c.	10.5	2.62	4.5	1.45	47.3	10.43	19.58	23.71	30	
Hypercalcemic										
12 a.	13.2	3.29	5.1	1.64	67.0	11.79	49.48	23.31		
b.	12.5	3.12	4.9	1.58	61.3	11.36	39.22	23.41	15	
c.	16.0	3.99	5.1	1.64	81.6	11.78	88.14	23.05		30
60 b.	17.0	4.24	3.0	0.97	51.0	6.97	37.03	23.43		
c.	16.8	4.19	2.9	0.93	48.7	6.69	32.97	23.48	45	
Hypocalcemic										
17 a.	7.8	1.95	6.9	2.22	53.8	15.96	18.84	23.73		
b.	8.2	2.05	7.2	2.32	59.0	16.68	23.93	23.62	71	
c.	4.1	1.02	8.1	2.61	33.2	18.77	3.81	24.41		

the ion product, $(Ca^{++})^3 \times (PO_4\equiv)^2$, is a more accurate criterion of the rate of deposition of $Ca_3(PO_4)_2$ than is the empiric Ca × P product.

It can be seen that the calcium and phosphorus product, or the $Ca_3(PO_4)_2$ ion product, or the negative logarithm of the $Ca_3(PO_4)_2$ ion product could not have been used as a prognostic index for the rate of ossification in these experiments. Although in dog 12 the ion product

9. Holt, L. Emmett; La Mer, Victor K., and Chown, Bruce H.: J. Biol. Chem. **64**:509, 1925.

10. Holt, L. Emmett: J. Biol. Chem. **64**:579, 1925.

is higher than in the other animals, it should be remembered that this product is to the negative twenty-fifth power, so that the actual difference is exceedingly small. The ion product in dog 17 was higher for a time than that of the control dogs, yet ossification took nearly twice as long.

In the control animals and in those fed on cod liver oil, ossification occurred within approximately the same period of time.

In the hypocalcemic animals, evidence of callus was not found in one dog after sixteen days; very slight callus was found in one dog after twenty-seven days; in the third animal, union was obtained in seventy-one days.[11]

Greenwald,[12] in 1926, and Hunter and Aub,[13] in 1927, found an increased excretion of calcium after the administration of parathyroid extract-Collip. The amount of calcium lost could have come only from the bones. Dog 60, which required forty-five days for union, refused food for some days when the serum calcium was maintained at a level of 18 or 19 mg. per hundred cubic centimeters, and only after reduction of the serum calcium did he again eat. It is possible that, on the inadequate diet, enough calcium was drained from the bones to delay ossification. It is our opinion that parathyroid extract should be used with caution in cases of fracture.

COMMENT

It is highly improbable that any single factor is the cause of nonunion in the majority of instances. In one instance it may be due to the interposition of soft parts; in another, to an inefficient blood supply at the site of fracture due to injury or location; in another, to damage to the periosteum, and in still another, it may be due to an insufficient amount of the inorganic constituents of the blood which take part in ossification.

Although a deficient inorganic phosphorus or calcium content of the serum may be the cause of abnormal or faulty ossification in the growing bone or in certain of the bone dyscrasis, it has been our experience that this factor is a rare one in the clinical patient with nonunion after fracture.

Robison[14] advanced the theory that calcification depends on the activity of an enzyme secreted by the osteoblasts and hypertrophic cartilage cells. He stated the belief that calcium and phosphorus exist in the blood and other tissue fluids partly as calcium phosphorus esters

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11. In this animal, the Ca-P product, the $Ca_3(PO_4)_2$ ion product and the negative logarithm of the $Ca_3(PO_4)_2$ ion product were within normal limits, except at the time of union when the ion product was considerably reduced, although the serum calcium concentration had dropped to about half its normal value.

12. Greenwald, Isidor, and Gross, Joseph: J. Biol. Chem. **68**: 325, 1926.

13. Hunter, Donald, and Aub, Joseph C.: Quart. J. Med. **20**: 123, 1927.

14. Robison, Robert: Biochem. J. **17**: 286, 1923.

and partly as tricalcium phosphate. The enzyme (phosphoric esterase) hydrolyses the ester, and liberates inorganic phosphorus which is deposited as $Ca_3 (PO_4)_2$. This theory is enticing, but as yet sufficient evidence has not been forthcoming to substantiate the fact that a deficient amount of esterase may account for some of the cases of nonunion after fracture.

In our own cases union occurred in every instance, with the exception of two animals (hypocalcemic) who did not live a sufficiently long time for ossification. In the one dog in which the serum calcium content was maintained at an abnormally low level, but whose phosphorus level had increased above normal, union occurred although it took approximately twice the average normal time. Surely if a low calcium content in itself is the cause of nonunion, it should have occurred in this animal. A deficient serum calcium in this case, however, produced delayed union. There is, however, the question as to whether or not a deficient serum calcium produced other than by thyroparathyroidectomy may result in nonunion. On this subject, we have no experimental data. We have not entered into a discussion of the diffusible and nondiffusible calcium in these animals.

SUMMARY

1. A study of the serum calcium and inorganic phosphorus after fractures in normal, hypercalcemic and hypocalcemic dogs is presented.

2. We have not been able to prognosticate the rate of ossification after fracture from the calcium and phosphorus product, from the ion product or from the negative logarithm of the ion product.

3. The marked decrease in serum calcium after thyroparathyroidectomy retarded ossification, although it did not prevent union.

PROTOCOLS

Dog 36.—Control (without cod liver oil).

March 21: Serum—Inorganic phosphorus = 2.9 mg. per hundred cubic centimeters.
Calcium = 11.6 mg. per hundred cubic centimeters.

March 23: Radius fractured.

April 2: X-ray picture showed slight periosteal reaction.

April 4: Serum—Inorganic phosphorus = 3.5 mg.
Calcium = 11.4 mg.

April 13: Serum—Inorganic phosphorus = 3.6 mg.
Calcium = 11.5 mg.

April 16: X-ray picture showed good external callus.

April 23: X-ray picture showed considerable callus with union.

Dog 48.—Control (no cod liver oil).

March 28: Serum—Inorganic phosphorus = 3.8 mg. per hundred cubic centimeters.
Calcium = 10.9 mg. per hundred cubic centimeters.

March 30: Fractured radius.
April 6: No callus.
April 11: Serum—Inorganic phosphorus = 3.5 mg.
Calcium = 11.3 mg.
April 16: No callus.
April 25: Serum—Inorganic phosphorus = 3.3 mg.
Calcium = 11.9 mg.
X-ray picture showed slight callus formation.
April 30: X-ray picture showed more external callus.

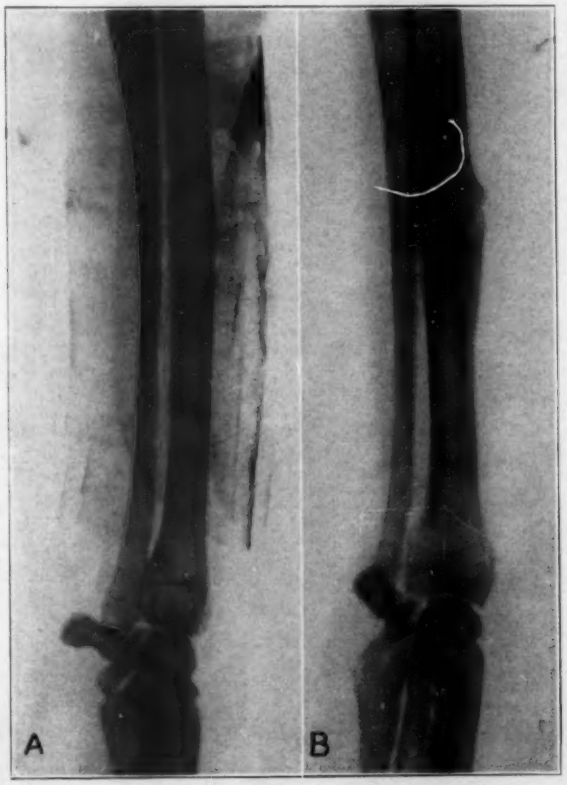

Fig. 1 (dog 36).—*A* shows the bone ten days after fracture; *B*, thirty days.

May 7: X-ray picture showed considerably more callus.
May 9: Serum—Inorganic phosphorus = 3.3 mg.
Calcium = 10.9 mg.
May 14: X-ray picture showed union.

Dog 10.—Cod liver oil control.
May 13: Serum—Inorganic phosphorus = 3.6 mg. per hundred cubic centimeters.
Calcium = 11.5 mg. per hundred cubic centimeters.
Fracture of radius.
May 25: Serum—Inorganic phosphorus = 3 mg.
Calcium = 10.7 mg.

June 2: X-ray picture showed very slight callus.

June 6: Serum—Inorganic phosphorus = 3.3 mg.
Calcium = 11.8 mg.
X-ray picture showed slight callus formation.

June 11: X-ray picture showed more callus.

June 20: X-ray picture showed considerable external callus with union.

Dog 22.—Cod liver oil control.

April 27: Fractured radius.

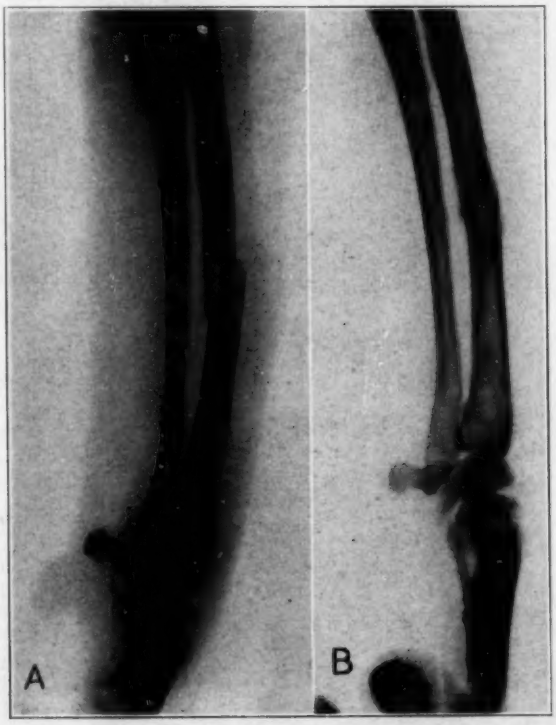

Fig. 2 (dog 48).—*A* shows the bone ten days after fracture; *B*, forty-five days.

April 29: Serum—Inorganic phosphorus = 4.7 mg. per hundred cubic centimeters.
Calcium = 11.7 mg. per hundred cubic centimeters.

May 7: X-ray picture showed very slight callus.

May 13: Serum—Inorganic phosphorus = 5.8 mg.
Calcium = 11.7 mg.

May 14: X-ray picture showed considerable external callus.

May 28: Serum—Inorganic phosphorus = 4.5 mg.
Calcium = 11.2 mg.

June 5: X-ray picture showed union with considerable external callus.

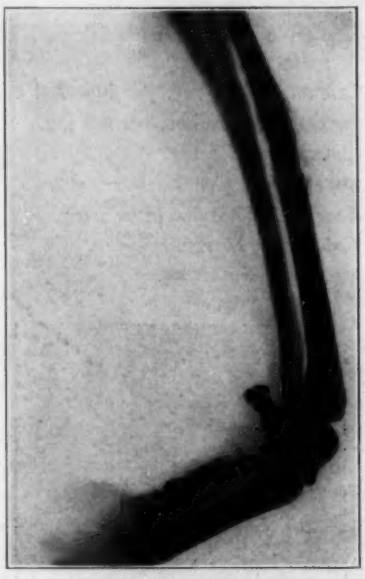

Fig. 3 (dog 10).—Thirty-six days after fracture.

Fig. 4 (dog 22).—*A* shows the bone ten days after fracture; *B*, thirty days.

Dog 12.—Hypercalcemic.

Feb. 21: Serum—Inorganic phosphorus = 5.2 mg. per hundred cubic centimeters.
Calcium = 11.8 mg. per hundred cubic centimeters.

March 7: Serum—Inorganic phosphorus = 4.6 mg.
Calcium = 11.5 mg.
10 units parathyroid extract.

March 9: Serum—Inorganic phosphorus = 5 mg.
Calcium = 14 mg.
10 units parathyroid extract.

Fig. 5 (dog 12).—Fifteen days after fracture.

March 11: Serum—Inorganic phosphorus = 4.9 mg.
Calcium = 11.8 mg.
10 units parathyroid extract.

March 14: Serum—Inorganic phosphorus = 5 mg.
Calcium = 11.3 mg.
30 units parathyroid extract.

March 16: Serum—Inorganic phosphorus = 5.1 mg.
Calcium = 13.2 mg.
40 units parathyroid extract.

March 18: Serum—Inorganic phosphorus = 4.9 mg.
Calcium = 12.5 mg.
50 units parathyroid extract.
Fracture of radius.

March 19 and 21: 50 units parathyroid extract each day.

March 23: Serum—Inorganic phosphorus = 4.8 mg.
Calcium = 11.9 mg.

March 25 and 27: 100 units parathyroid extract each day.

March 28: Serum—Inorganic phosphorus = 5.1 mg.
Calcium = 16 mg.

March 30: 10 units parathyroid extract.

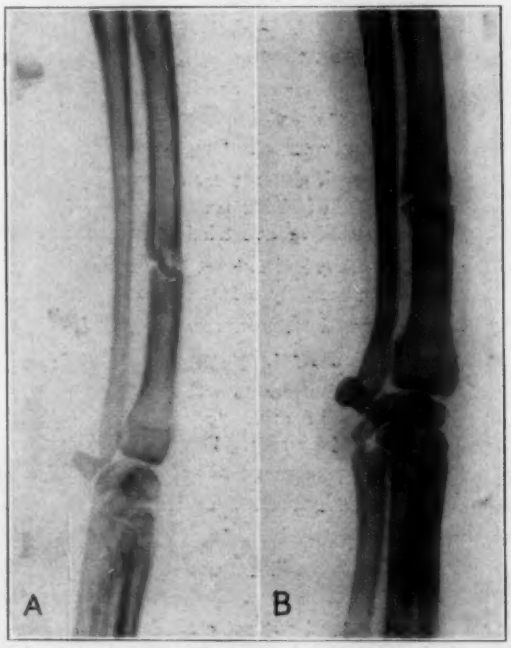

Fig. 6 (dog 60).—*A* shows the bone ten days after fracture; *B*, forty-five days.

March 31: 40 units parathyroid extract.

April 1: Serum—Inorganic phosphorus = 13.4 mg.
Calcium = 4.7 mg.

April 2: X-ray picture showed definite evidence of union. Dog able to walk without limp, no crepitation.

Dog 60.—Hypercalcemic.

April 19: 100 units parathyroid extract.

April 20: Serum—Inorganic phosphorus = 3 mg. per hundred cubic centimeters.
Calcium = 17 mg. per hundred cubic centimeters.
Fracture of radius.

April 22: Serum—Inorganic phosphorus = 12.2 mg.
Calcium = 3.9 mg.
80 units parathyroid extract.

April 24: 100 units parathyroid extract.

April 25: Serum—Inorganic phosphorus = 11.6 mg.
Calcium = 3.9 mg.
100 units parathyroid extract.

April 27: Serum—Inorganic phosphorus = 4.1 mg.
Calcium = 13 mg.

April 28: 100 units parathyroid extract.

April 30: Serum—Inorganic phosphorus = 4.1 mg.
Calcium = 18.9 mg.
Very slight callus.

May 1: 100 units parathyroid extract.

May 2: Serum—Inorganic phosphorus = 4.2 mg.
Calcium = 19.2 mg.

May 3: 100 units parathyroid extract. Dog not eating.

May 5-7: 100 units parathyroid extract each day.
X-ray picture showed slight periosteal callus.
Dog not eating well. Have tried alteration of diet with no result.

May 9-11-13: 100 units parathyroid extract each day. Dog still not eating his food. Takes only a small amount of milk.

May 14: X-ray picture showed some increase in callus.

May 15-17: No parathyroid extract.

May 18: Serum—Inorganic phosphorus = 2 mg.
Calcium = 11.6 mg.
80 units parathyroid extract. Dog trembling; thin and looks sick. There is a high percentage of red cells to the serum.

May 20: 80 units parathyroid extract. Dog is eating better last two days.

May 21: Condition much improved.

May 22-24-26: 80 units parathyroid extract each day. Dog much improved; eating well.

May 28-30: 80 units parathyroid extract each day.
X-ray picture showed more callus. Parathyroid extract each day.

June 1-3: Dog in splendid condition.

June 5-7: 80 units parathyroid extract each day.
Serum—Inorganic phosphorus = 2.9 mg.
Calcium = 16.8 mg.
X-ray picture showed bone united with considerable internal and external callus.

Dog 17.—Hypocalcemic.

Feb. 7: Started feeding 20 cc. cod liver oil daily.

Feb. 14: Serum—Inorganic phosphorus = 5.7 mg. per hundred cubic centimeters.
Calcium = 11.2 mg. per hundred cubic centimeters.

Feb. 25: Serum—Inorganic phosphorus = 5.9 mg.
Calcium = 11.6 mg.

March 2: Serum—Inorganic phosphorus = 5.4 mg.
Calcium = 11.7 mg.

March 11: Removed most of parathyroid glands.

March 14: Serum—Inorganic phosphorus = 5.5 mg.
Calcium = 10.6 mg.

March 16: Serum—Inorganic phosphorus = 5.5 mg.
Calcium = 10.8 mg.

March 21: Removed all of parathyroid and thyroid glands.

Fig. 7 (dog 17).—*A* shows the bone ten days after fracture; *B*, seventy days.

March 23: Serum—Inorganic phosphorus = 6.9 mg.
Calcium = 7.8 mg.

March 25: Serum calcium = 6.5 mg.
Fractured radius.

March 28: Slight attack of tetany.
Given 1 cc. of parathyroid extract, which relieved attack.

March 29: Slight attack of tetany.
Given 1 cc. of parathyroid extract, which relieved attack.

April 1: Dog in good condition.
Serum—Inorganic phosphorus = 7.2 mg.
Calcium = 8.2 mg.

April 4: X-ray picture showed very slight callus.

April 11: Dog in splendid condition.
Serum—Inorganic phosphorus = 7.3 mg.
Calcium = 7.7 mg.
X-ray picture showed slight external callus.

April 23: Slight increase in external callus.

April 25: Condition splendid.
Serum—Inorganic phosphorus = 8.8 mg.
Calcium = 5.4 mg.

April 30: Further increase in external callus.

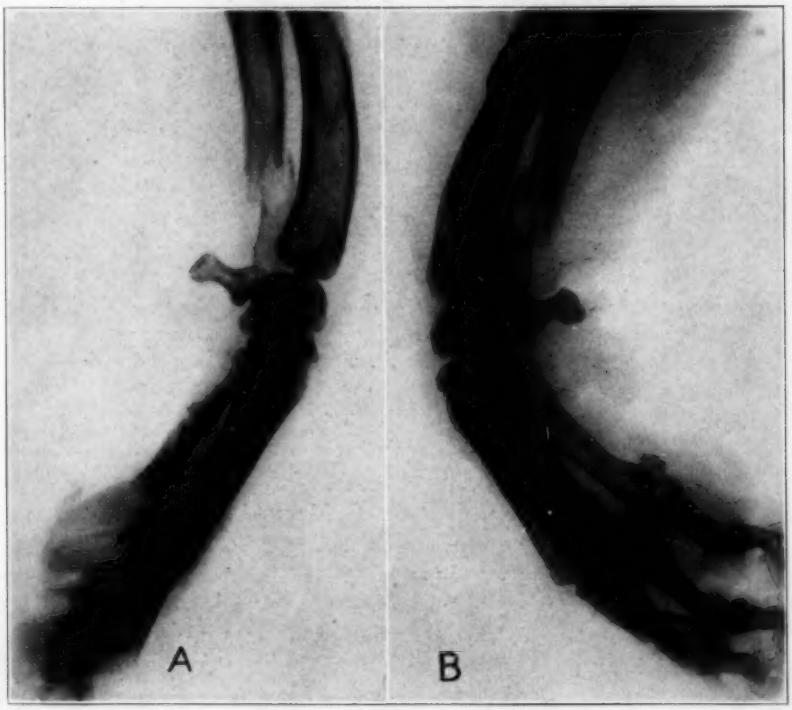

Fig. 8 (dog 27).—*A* shows the bone ten days after fracture; *B*, sixteen days.

May 7: X-ray picture showed considerable external callus.

May 14: X-ray picture showed increase in external callus.

May 28: X-ray picture showed fracture almost united.

June 1: Excellent condition.
Serum—Inorganic phosphorus = 8.1 mg.
Calcium = 4.1 mg.

June 4: X-ray picture showed union.
Dog killed 186 days after operation. Condition excellent.

Dog 27.—Hypocalcemic.

Feb. 7: Started feeding 20 cc. cod liver oil daily.

Feb. 25: Serum—Inorganic phosphorus = 3.1 mg. per hundred cubic centimeters.
Calcium = 10.2 mg. per hundred cubic centimeters.

Feb. 28: Thyroparathyroidectomized.

March 2: In tetany.
Gave cod liver oil and 20 units of parathyroid extract.

March 4: Shivering. Gave 10 units of parathyroid extract.

Fig. 9 (dog 15).—*A* shows the bone ten days after fracture; *B*, twenty-seven days.

March 7: Serum—Inorganic phosphorus = 4 mg. Animal not in tetany, but not in good condition.
Calcium = 5 mg.
Condition improved.

March 9: Fractured radius and ulna.

March 11: Serum—Inorganic phosphorus = 3.9 mg.
Calcium = 5.3 mg.
Poor condition; not eating.

March 13: Poor condition. Not eating his food.
Put on diet of anything he would eat. No active tetany.

March 19: X-ray picture did not show evidence of callus.

March 25: X-ray picture did not show evidence of callus. Died after considerable loss of weight from lack of food. No attempt was made to force diet. Animal was not in tetanic spasm since March 2.

Dog 15.—Hypocalcemic.

April 16: Started feeding 20 cc. cod liver oil daily.

May 2: Thyroparathyroidectomized.

May 4: Serum—Inorganic phosphorus = 7.5 mg. per hundred cubic centimeters.
Calcium = 8.2 mg. per hundred cubic centimeters.

May 4: Fracture of radius.

May 6: Serum—Inorganic phosphorus = 7.8 mg.
Calcium = 5.9 mg.

May 11: Condition fair. Slight weakness and eyes sore-looking. No sign of tetany.
Forced feeding of milk but not much food retained.
Serum—Inorganic phosphorus = 8.7 mg.
Calcium = 5.3 mg.

May 13: Weak, blind from bilateral cataract. No tetany.
Given 20 units of parathyroid extract.

May 14: X-ray picture did not show evidence of callus.

May 18, 9 a. m.: Very good condition now, except for sore eyes.
Drank milk voluntarily.
11 a. m.: Severe attack of tetany.
Given 20 units of parathyroid extract.

May 20: Condition better.

May 23: Condition considerably improved.

May 25: Severe conjunctivitis.

May 26: Eyes in bad condition.
Serum—Inorganic phosphorus = 7.5 mg.
Calcium = 3.3 mg.

May 30: Slight callus.

May 31: Died after gradual loss of weight and inanition. No tetany.

INTRAMEDULLARY LIPOMA OF THE SPINAL CORD

COMPLETE OPERATIVE REMOVAL *

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AND

EDGAR F. FINCHER, JR., M.D.

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ST. LOUIS

Intramedullary lipoma of the spinal cord is extremely rare clinically. Because of its rarity and also because it was possible to remove the tumor at operation, it has been deemed desirable to report this case.

REPORT OF A CASE

History.—J. M., a man, aged 46, entered Barnes Hospital in February, 1928, complaining of weakness in the lower extremities. The onset occurred three years prior to entrance, with pain in both ankles and in the right knee. Although pain was without relation to motion, he was treated for arthritis for six months. When not standing, he was free from discomfort. Weakness soon intervened, and he had been incapacitated for work during the past eighteen months of his illness. A year before he entered the hospital, the pain had almost subsided but weakness gradually progressed, so that walking was possible only with considerable difficulty. The outstanding feature was an inability to lift his feet. Marked subjective sensory disturbances or altered bladder or rectal function had never been present.

Examination.—There was a diminution in sensation to light touch, pinprick, heat and cold, from the twelfth dorsal skin segment down. A band of complete anesthesia, corresponding to the tenth and twelfth dorsal skin segment, was present. The abdominal reflexes were absent and the cremasteric reflexes rather feeble. The patellar and ankle jerks were increased. A bilateral Oppenheim sign was elicited. There was a slight spasticity of the lower extremities, but patellar or ankle clonus was not present. The rest of the physical examination gave negative results.

Diagnosis.—Lumbar puncture with a water manometer showed a spinal fluid pressure of 19 cm. Ten-second bilateral jugular compression increased the fluid pressure to 29 cm. When the jugular pressure was released, the spinal fluid returned to 19 cm. within ten seconds. The fluid came down to normal in a steppage fashion. This was interpreted as a partial block of the spinal fluid. Laboratory examination of the fluid was normal throughout.

Later, an injection of iodized oil 40 per cent was made. X-ray examination showed that the greater part of the 1.5 cc. of oil, injection of which had been made into the cisterna magna, had dropped to the bottom of the canal. However, in the mid-dorsal region, streaks of oil were lodged on each side of the canal. The point at which the globules were lodged corresponded to the level of the lesion as determined by neurologic examination.

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Operation.—The usual laminectomy procedure was carried out. The fifth, sixth, and seventh dorsal spinous processes were removed. There was no extra dural fat. The dura did not pulsate, and at the place where there was a fusiform enlargement, the dura had a yellowish tinge, as shown in figure 1 *A*. When the dura was opened, the cord was found distended by a yellowish mass beneath the arachnoid which had running over it fine longitudinal bands of tissue from the spinal cord. The appearance is well illustrated in figure 1 *B*. A longitudinal incision was made over this mass after one vessel that ran over the cord had been clipped. Careful retraction of the incised tissue finally revealed an encapsulated lipoma which was readily peeled out of the substance of the cord (fig. 1 *C*).

After the tumor had been removed, a shallow ovoid cavity remained in the cord. As the field was perfectly dry, the dura was closed with fine silk and the wound was closed in layer sutures in the usual way.

Discharge.—The patient was discharged from the hospital two weeks after operation. There was spasticity of the lower extremities just as there had been before operation, but he was able to walk with the aid of a cane.

Pathologic Examination.—The tumor weighed 2.25 Gm., was 2.5 cm. long and 1 cm. in diameter; it was nodular, encapsulated, moderately firm and whitish-yellow. Sections from different parts of the specimen showed that it was composed entirely of fat tissue (fig. 2). There were few small blood vessels, but one large one was found in every section. The capsule of the tumor was moderately thick and was composed of a dense connective tissue (fig. 3). Specific stains on sections from different areas of the tumor did not show neural or glial elements.

COMMENT

A more definite conception of the rarity of intramedullary lipomas of the spinal cord may be gained from their incidence in the large collections of tumors of the cord reported by various authors. In the well known monograph by Gowers and Horsley [1] on the first successfully removed tumor of the spinal cord, the authors reported fifty-eight cases collected from the literature. The occurrence of an intramedullary lipoma is not recorded by them.

In 100 tumors studied by Elsberg,[2] fourteen were intramedullary. Not one of the fourteen was a lipomatous growth. Steinke [3] collected reports of 330 tumors of the cord for Frazier, and no case of intramedullary lipoma is found in this large group.

In a series of 112 laminectomies reported by Adson and Ott [4] for focal symptoms of disease of the cord, not a single case of lipoma within the cord was found. In 156 laminectomies performed at Barnes Hos-

1. Gowers, W. R., and Horsley, V.: A Case of Tumor of the Spinal Cord; Removal; Recovery, M. Chir. Trans., London, 1888, vol. 71, p. 377.

2. Elsberg, Charles: Tumors of Spinal Cord, New York, Paul B. Hoeber, Inc., 1925.

3. Steinke, C. R.: Spinal Tumors. Statistics on a Series of 330 Collected Cases, J. Nerv. & Ment. Dis. **47**:418, 1918.

4. Adson, A. W., and Ott, W. O.: Results of Removal of Tumors of the Spinal Cord, Arch. Neurol. & Psychiat. **8**:520 (Nov.) 1922.

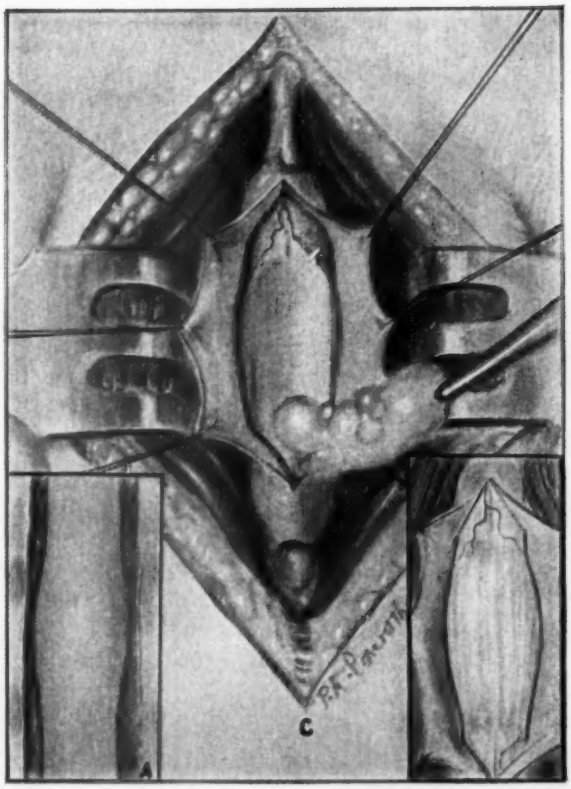

Fig. 1.—*A* shows the fusiform enlargement on dura; *B*, after dura was opened, appearance of cord which was distended by a yellowish mass beneath the arachnoid; *C*, encapsulated lipoma which was readily peeled out.

pital for localized symptoms of disease of the cord, this is the first intramedullary lipoma encountered.

The rarity of this type of lesion was still more strikingly emphasized only a few months ago by Stookey [5] in an article on lipomas of the spinal cord. He was able to find reports of only nine cases in the literaure, to which he added one of his own.

A critical review of the cases he reported leads us to feel that the cases reported by Gowers,[6] Turner [7] and Wolbach [8] cannot truly be

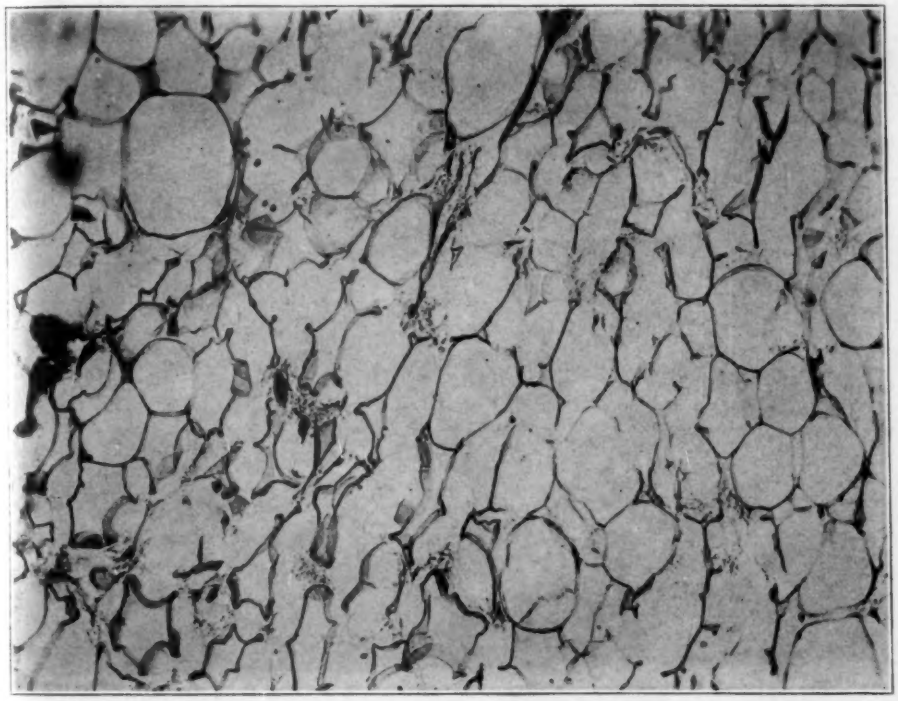

Fig. 2.—Characteristic fat cells found throughout the tumor. Phosphotungstic acid stain; × 160.

called pure lipomas. In Gowers' case the author himself termed the tumor a myolipoma, since it contained muscle fibers. We are inclined

5. Stookey, Byron: Intradural Spinal Lipoma, Arch. Neurol. & Psychiat. **18**:16 (July) 1927.

6. Gowers, W. R.: Myolipoma of the Spinal Cord, Tr. Path. Soc. London, 1876, p. 27.

7. Turner, C.: Lipomatous Tumor (Sarcoma) of Spinal Cord, Tr. Path. Soc. London, 1888, p. 25.

8. Wolbach, S. B., and Millet, J. A. P.: Diffuse Subdural Lipomatosis of Spinal Cord in an Infant, Boston M. & S. J., 1913, p. 168.

to accept Wolbach's idea that this tumor was associated with a spina bifida. In Turner's case, the description is that of a fibronuclear tumor containing fat cells and was considered by him a sarcomatous growth. Wolbach prefers the term diffuse subdural lipomatosis of the spinal cord in his case. In view of the fact that this was associated with other congenital anomalies, it seems probable to us, as it did to the author, that this was just another congenital defect.

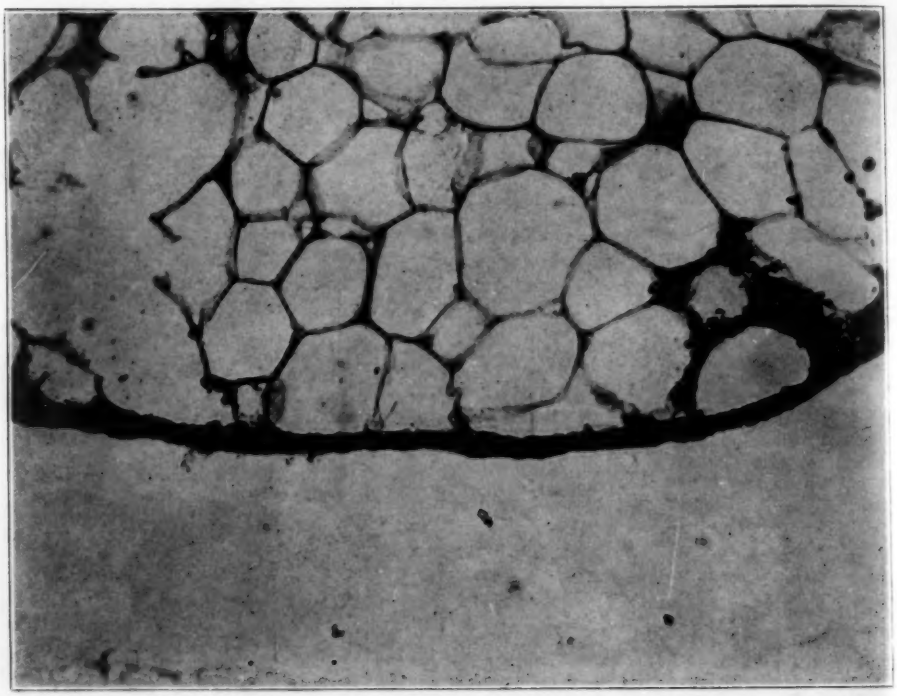

Fig. 3.—Capsule that entirely surrounded the tumor. Phosphotungstic acid stain; × 300.

In the remaining seven cases from the literature (Branbach,[9] Spiller, Thomas,[10] Ritter,[11] Stookey,[5] Oppenheim and Borchardt[12] and

9. Branbach: Ein fall von Lipom bildung der Rückenmarks haüte, Arch. f. Psychiat. **15**:489, 1899.

10. Thomas, S., and Jumentie, J.: Lipome de cone terminale, Rev. neurol. **21**: 222, 1912.

11. Ritter, A.: Ein Lipoma der Meningen des Cervicalmarks, Deutsche. Ztschr. f. Chir. **152**:189, 1920.

12. Oppenheim, H., and Borchardt, M.: Weitere Beitrag zur Erkennung und Behandlung des Ruckenmarks-geschwülste, Deutsche. Ztschr. f. Nervenh. **60**:1, 1918.

Root[13]) the tumors were all pure lipomatous growths. They differ, however, from the case reported here in that they were all apparently infiltrative and not encapsulated.

Stookey discussed at some length the various theories as to the origin of intramedullary lipomatous growths. He does not seem to favor one theory more than another. The fact that in the case here presented the entire tumor was located beneath the arachnoid seems to lend support to the view held by Virchow that it arose from cell rests which became hypertrophic.

The treatmcnt for this type of lesion based on previously reported cases has been against too persistent attempts at removal. As complete enucleation was carried out in this case, we feel that in the future it would be worth while to consider such a procedure in every case. At first inspection in this case the removal of the tumor seemed impossible, but careful manipulation at the sacrifice of a few fibers of the cord finally showed its feasibility. Lipoma is one of the most benign types of lesions, and the removal always holds out a better prognosis for the patient. This, we think, makes it justifiable to do a partial extirpation in all persons with lipoma of the spinal cord when complete removal is not possible.

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13. Root, E. F.: A Case of Lipoma of Spinal Cord, Utah M. J., 1906-1907, p. 40-42.

THE BACTERICIDAL PROPERTIES OF THE SOLUTION S.T. 37 (LIQUOR HEXYLRESORCINOLIS 1:1,000) *

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This paper is the second [1] in which the results of experiments having a two-fold object are presented. The experiments were made to determine (1) the action of several of the more frequently used antiseptics on some of the more common pathogenic organisms and (2) the reliability of the present standard of evaluating antiseptics as a means of correct appraisal of their practical value. A more detailed report may be expected in a later communication.

In May, 1927, Leonard and Feirer [2] described a new antiseptic known as S.T. 37. It is a practically colorless, odorless, limpid fluid with a warm, sweetish taste, containing 1 mg. of crystalline hexylresorcinol per cubic centimeter of solvent, consisting of 30 per cent glycerin and 70 per cent water. This solution is claimed [3] to be bactericidal to viable bacterial suspensions in fifteen seconds or less. It is further stated to be nontoxic, nonirritating, chemically stable, bactericidal in high dilution, highly penetrating, noncorrosive and nonstaining, and is free from disagreeable odor. Such an antiseptic would be welcomed by the surgeon, especially by the surgeon dealing with traumatic cases, the majority of which come to him in a contaminated condition. Therefore, at the suggestion of Dr. John J. Moorhead, professor of surgery at the New York Post-Graduate Medical School and Hospital, the investigation of this substance was undertaken.

S.T. 37 is an outgrowth of experimentation with resorcinol and allied preparations. The first clinical descriptions [4] of the use of hexylre-

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* From the Department of the Laboratories, New York Post-Graduate Medical School and Hospital.

1. Wright, Irving S.: Effects of Mercurochrome-220 Soluble on the Growth of *Bacillus pyocyaneus*, Arch. Surg. **15**:958 (Dec.) 1927.

2. Leonard, Veader, and Feirer, W. A.: Bactericidal Activity of Hexylresorcinol in Glycerine, Bull. Johns Hopkins Hosp. **41**:21 (May) 1927.

3. Leonard, Veader, and Feirer, W. A.: (footnote 2); Hexylresorcinol as a General Antiseptic, Surg. Gynec. Obst. **45**:603 (Nov.) 1927.

4. Leonard, Veader: Secretion of Bactericidal Urine and the Disinfection of the Urinary Tract, J. A. M. A. **83**:2005 (Dec. 20) 1924. Henline, R. B.: Hexylresorcinol in the Treatment of 50 Cases of Infection of the Urinary Tract, J. Urol. **14**:119 (Aug.) 1925. Brown, D. A.: Hexylresorcinol in Infection of the Urinary Tract, J. A. M. A. **86**:668 (March 6)1926. Scott, W. J., and Leonard, Veader: Hexylresorcinol in the Treatment of Pyelitis of Infancy and Childhood, Am. J. Dis. Child. **31**:241 (Feb.) 1926. Wynne, H. M. N.: Hexylresorcinol in Urinary Tract Infection in Women, Minn. Med. **9**:156 (April) 1926. Leonard, Veader: Hexylresorcinol, J. Urol. **12**:585 (Oct.) 1924.

sorcinol in the treatment of the more common types of infections of the urinary tract indicated excellent results. Later reports from other clinicians [5] presented varying degrees of success and failure resulting from its use. In investigating these reports, Leonard, Frobisher and Wood [6] found that certain definite physical factors were involved. They noted that surface tension played a real part in determining the clinical efficacy of the drug. With the ingestion of large amounts of water, sodium bicarbonate or citrates, in conjunction with the hexylresorcinol, a urine of high surface tension and of low bactericidal quality was voided. Reduction of the surface tension of the urine, by preventing the simultaneous use of excessive fluids, bicarbonates and citrates, improved the clinical results obtained with this drug. In fact, the urine itself then possessed a relatively high bactericidal titer [7] following the ingestion of 0.6 Gm. of hexylresorcinol three times daily. This manifestation was attributed to the presence of the drug plus the low surface tension.

In March, 1927, Frobisher [8] demonstrated definitely the effect of surface tension on the action of antiseptics. By lowering or raising the surface tension phase of a solution of phenol, he could appreciably increase or decrease, respectively, the bactericidal potency of the same antiseptic. Within a few months, Leonard and Feirer [3] described the antiseptic which is the subject of this paper.

Hexylresorcinol, per se, has a phenol coefficient of from 43 to 56 according to the United States Public Health Standard, as quoted by Dr. Swenarton.[9] It is readily soluble in glycerin, but sparingly soluble in water. It combines high bactericidal qualities and low toxicity better than any other similar phenolic preparation. Both solvents have a surface tension in excess of 70 dynes per centimeter, while hexylresorcinol

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5. Helmholtz, H. F.: The Therapeutic Value of Hexylresorcinol in Chronic Pyelitis of Children, Am. J. Dis. Child. **32**:396 (May) 1926. Eberbach, C. W., and Arn, R. D.: Hexylresorcinol in Urinary Tract Infections; Therapeutic Effect, J. A. M. A. **89**:512 (Aug. 13) 1927.

6. Leonard, Veader, and Frobisher, Martin, Jr.: linical Application of Hexylresorcinol in Urology with Observation on the Significance of Surface Tension in Urinary Antisepsis, J. Urol. **15**:1 (Jan.) 1926. Leonard, Veader: Diuresis Versus Antisepsis in the Treatment of Urinary Tract Infections with a Note on Drug Rotation, J. A. M. A. **80**:517 (Aug. 13) 1927. Leonard, Veader, and Wood, Austin: Present Status of Hexylresorcinol as an Internal Urinary Disinfectant, J. A. M. A. **85**:1855 (Dec. 12) 1925.

7. Leonard, Veader (footnote 4, first reference). Leonard, Veader, and Feirer, W. A.: Stability of Hexylresorcinol in Pharmaceutical Preparations, J. Phar. & Exper. Therap. **28**:395 (Sept.) 1926.

8. Frobisher, Martin, Jr.: Studies upon the Relationship Between Surface Tension and the Activity of Disinfectants, with Special Reference to Hexylresorcinol, J. Bact. **13**:163 (March) 1927.

9. Swenarton, J. C., in Leonard, Veader (footnote 4, first reference).

is in itself a surface tension reducent. After trying various combinations of the drug, water and glycerin, Leonard and Feirer prepared S.T. 37. This preparation has the lowest surface tension combined with the greatest bactericidal action of any of the many alkylated resorcinol derivatives in varying solvent combinations investigated. Its name signifies a solution the surface tension of which (S.T.) is 37 dynes per centimeter.

Leonard and Feirer used the following protocol [2] to determine the bactericidal efficacy of S.T. 37: Fresh twenty-four hour cultures of the several test organisms were used. A standard 3 mm. loopful of inoculum was introduced into 5 cc. of S.T. 37, from which similar transplants were made to 10 cc. of broth and incubated at 37 C. for twenty-four hours. The transplants were made after fifteen, thirty and sixty seconds, respectively. Suitable controls were made. Failure to obtain growth in the transplants using fifteen different organisms was taken as conclusive evidence that S.T. 37 was bactericidal for those organisms in fifteen seconds or less.

Our preliminary experiments were made with *Bacillus pyocyaneus,* one of the organisms for which S.T. 37 was claimed to be bactericidal in fifteen seconds or less. This work demonstrated to us that the organism of green pus was viable after having been in continuous contact with full strength S.T. 37 for a period in excess of forty-eight hours.

For the detailed experiments to be presented, the organisms used were laboratory stock strains of *Bacillus pyocyaneus (Pseudomonas pyocyanea)* and *Staphylococcus aureus,* and a strain of hemolytic streptococcus isolated from the blood of a patient with septicemia following mastoiditis. The cultures before being used were transplanted on agar for five successive days preceding experimentation.

Meat infusion agar slants were used except in the case of *Streptococcus hemolyticus.* For this, the brain agar mediums of Pelouze and Viteri [10] was used, on which the control cultures of the streptococcus grew luxuriantly. The broth was the standard meat infusion dextrose broth. The spinal fluid medium was a mixture of specimens sent to the laboratory for routine examination from patients suffering from meningococcus meningitis or streptococcus meningitis. This fluid was heated at 60 C. Sterility was later proved by absence of growth after forty-eight hours of incubation on agar and in broth. That this medium would support growth was shown by control cultures.

Two different samples of S.T. 37 were used in our work. One was an original 3 ounce bottle; the other was a portion of a similar 12 ounce bottle. Both of these samples were obtained from the Hospital Pharmacy.

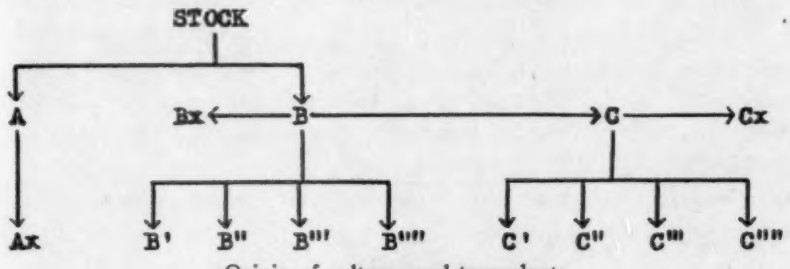
With each organism six experiments were performed to ascertain the effect of S.T. 37 under various conditions: (1) undiluted S.T. 37 on a twenty-four hour growth on agar slant; (2) undiluted S.T. 37 applied immediately to a freshly inoculated agar slant; (3) S.T. 37 diluted 1:1 applied to the twenty-four hour growth in spinal fluid; (4) S.T. 37 diluted 1:1 applied to spinal fluid immediately

10. Pelouze, P. A., and Viteri, L. E.: A New Medium for Gonococcus Culture, J. A. M. A. **86**:684 (March 6) 1926.

after inoculation; (5) S.T. 37 diluted 1:2 applied to the twenty-four hour growth in broth; (6) S.T. 37 diluted 1:2 applied immediately to the freshly inoculated broth culture.

For each organism the following procedure was used, except as specially noted. From the fifth daily successive transplant, two tubes were inoculated and incubated at 37 C. for twenty-four hours. The next day, tube *Ax* was planted from *A* to prove the viability of *A*; these two were subsequently used as comparators and controls of growth. From tube *B*, two new transplants were made; *Bx*, a transplant from *B* to prove the viability of *B*, and tube *C*, which was a fresh inoculation. As soon as it was possible after inoculating *C*, *Cx* was inoculated as a control of *C*, being planted on agar. S.T. 37 was immediately added to both *B* and *C* tubes, the whole procedure requiring approximately one minute between the time of inoculating *C* and adding to it the antiseptic. Tubes *A*, *Ax*, *Bx* and *Cx* were incubated at 37 C. for twenty-four hours, and served as controls.

Experiments *B* and *C* were further conducted as indicated in the accompanying figure. At the end of intervals, measuring from time of addition of the S.T. 37, one loopful of the fluid culture medium with its recent admixture of antiseptic was streaked on an agar slant and recorded with the time as *B'*, *B"*, or *C'*, *C"*, etc.



Origin of cultures and transplants.

From the original agar slant cultures a similar loopful of material from the agar surface, below the antiseptic, was streaked on the respective agar slants as already described. In the latter group of experiments, sufficient S.T. 37 was added to the original agar slant *B* and *C*, to immerse totally the upper portion of the slant when held in the vertical position. The aforementioned transplants were incubated at 37 C., examined and recorded at the end of twenty-four and forty-eight hours.

In the experiments with *Bacillus pyocyaneus*, the time intervals of the *B* and *C* replants were one, two, four, twenty-four and forty-eight hours. The results at the end of the proper incubation period were outstanding (table 1). All the controls were definitely positive. All of the *B* and *C* series showed a positive growth of organisms after having been in contact with the S.T. 37 solution, either concentrated as on the agar or diluted 1:1 as in the spinal fluid or 1:2 as in the broth, even after forty-eight hours of continuous contact. From this series of experiments, it is concluded that S.T. 37 is not effectively bactericidal for *Bacillus pyocyaneus* in fifteen seconds or even in forty-eight hours.

Preliminary work done with *Staphylococcus aureus* and *Streptococcus hemolyticus* led us to believe they were not as resistant as the organism of green pus. In the next two series, exactly the same procedure was used as that already mentioned except in the time intervals of the transplants. With these bacteria, the transplants were made at the end of fifteen and thirty minutes, and one and one-half and two and one-half hours after the addition of the antiseptic.

The results were as follows: All of the controls of the two pathogens were positive, as would be anticipated. None of the streptococcus replants showed any growth, proving the bactericidal effect of S.T. 37 on *Streptococcus hemolyticus* in fifteen minutes or less, whether the antiseptic be full strength or diluted 1:2. However, the replants from the

TABLE 1.—*Effect of S. T. 37 on Bacillus Pyocyaneus*

Organism	Bacillus pyocyaneus (Pseudomonas pyocyanea)					
Medium	Agar		Spinal Fluid		Broth	
Dilution of S.T. 37	Undiluted		1:1		1:2	
Age of culture	24 Hours	1 Minute	24 Hours	1 Minute	24 Hours	1 Minute
Time Interval of Transplants in Hours:						
1	+	+	+	+	+	+
2	+	+	+	+	+	+
4	+	+	+	+	+	+
24	+	+	+	+	+	+
48	+	+	+	+	+	+

TABLE 2.—*Effect of S. T. 37 on Streptococcus Hemolyticus*

Organism	Streptococcus hemolyticus					
Medium	Agar		Spinal Fluid		Broth	
Dilution of S.T. 37	Undiluted		1:1		1:2	
Age of culture	24 Hours	1 Minute	24 Hours	1 Minute	24 Hours	1 Minute
Time Interval of Transplants in Minutes:						
15	0	0	0	0	0	0
30	0	0	0	0	0	0
90	0	0	0	0	0	0
150	0	0	0	0	0	0

TABLE 3.—*Effect of S. T. 37 on Staphylococcus Aureus*

Organism	Staphylococcus aureus					
Medium	Agar		Spinal Fluid		Broth	
Dilution of S.T. 37	Undiluted		1:1		1:2	
Age of culture	24 Hours	1 Minute	24 Hours	1 Minute	24 Hours	1 Minute
Time Interval of Transplants in Minutes:						
15	+	0	+	0	+	0
30	0	0	0	0	+	0
90	0	0	0	0	0	0
150	0	0	0	0	0	0

twenty-four hour growth of *Staphylococcus aureus* were positive in the fifteen-minute tubes of all three mediums, and positive as well in the broth replant at the end of the thirty-minute period (table 3). None of the fresh (*C* tubes) of *Staphylococcus aureus* replants showed any growth. Hence, S.T. 37 is bactericidal to *Staphylococcus* in either concentrated form or diluted 1:2 in some time under ninety minutes.

In a previous paper, one of us (I. S. W.) [1] showed that murcurochrome-220 soluble is ineffective as a germicide against *Bacillus pyocyaneus,* while tincture of iodine killed the same organism under exactly the same conditions. The number of antiseptics and other bactericidal preparations is well known to the medical profession. Many have been proposed with a statement of their phenol coefficient, and from this, with or without sufficient experimental proof, their respective bactericidal properties have been claimed. As one reviews the literature of antiseptics and as one notes the actual efficacy of antiseptics, one is led to question the value of the phenol coefficient as a standard for the proper evaluation of modern antiseptics for practical use.

CONCLUSIONS

1. S.T. 37 is not effectively bactericidal for *Bacillus pyocyaneus* in forty-eight hours or less.

2. S.T. 37 is bactericidal for *Staphylococcus aureus* in some time under ninety minutes.

3. S.T. 37 destroys *Streptococcus hemolyticus* in less than fifteen minutes.

4. S.T. 37 is stable and active in spinal fluid.

THE FUNCTION OF THE DIAPHRAGM*

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The relationship between the action of the diaphragm and the intercostal muscles, as well as the muscles of less importance, in making respiration possible by rhythmically enlarging and decreasing the volume of the thoracic cavity has been the subject of discussion by clinicians, surgeons and physiologists. Many valuable observations have been made which, at the present time, form a background for further observation and a fund of information from which to draw, as need arises, during the progress of research. In time, certain fixed opinions become accepted as facts, often because they are stated with emphasis, owing to the conviction of their authors. As truth is relative and corresponds with the best thought of a period, these opinions are true unless they can be proved incorrect, inaccurate or incomplete.

For one to replace an old truth by a wider and more accurate conception of fact requires that the observer make use of all available information and therefore include a survey of the embryologic, anatomic, physiologic and clinical knowledge of others as well as his own. In this survey the action and purpose of the diaphragm as a respiratory organ will be considered from these several points of view, from each of which, it is believed, valuable implications will be discovered.

EMBRYOLOGY

Prentis and Arey, Ballantyne, Keibel, Hume and Mall agree that the development of the diaphragm is a complex and obscure part of organogenesis, and that it is derived from sources other than the septum transversum in which His recognized its anlage, the most important being the pericardiopleural and the pleuroperitoneal membranes. All observers agree that the beginning of the diaphragm is in the early development of the embryo (the third week of which is so picturesquely described by Ballantyne), that its origin is high toward the head and that it migrates caudally and occupies different planes as it passes into the celom to become one of the most important structures which divide it into its several compartments.

Thus, the first chief partition has been the anlage of the diaphragm recognized by His in a mass of mesoblastic tissue situated, with the

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heart, among structures belonging to the head and containing within it the veins to the heart as well as the anlage of the liver, which he described as the septum transversum.

The second primitive structure passing inward to join with the septum to form the permanent partition is that which Mall described as extending from the lobe of the liver along the dorsal wall of the ductus cuvieri to the dorsal attachment of the mesocardium. Later this structure grows toward the head to complete the pericardiopleural membrane and then toward the tail to complete the pleuroperitoneal membrane. It is the pulmonary ridge which really is "an extension of the septum transversum from the lobes of the liver to the tip of the wolffian body." With the shift of the heart and liver as growth progresses and the accompanying migration of the dorsal end of the septum transversum toward the tail, the pulmonary ridge grows and divides into two membranes, one of which contains the phrenic nerve. This motor nerve enters the structures which ultimately produce the mature diaphragm opposite the fifth cervical segment. At the same level the striated muscle takes origin from masses from which muscle will develop later, which lie on each side of that segment.

In Broman's diagram, five points of origin are shown: (1) the septum transversum, (2) and (3) derivatives of mesentery, (4) derivatives of pleuroperitoneal membrane and (5) parts derived from the wall of the body. All except the last have been discussed. The last is mentioned because of the contention between two opposing schools. One believes that there is more than one motor nerve supplying the diaphragm; the other is of the opinion that the phrenic nerve is the only nerve supplying motor impulses to the diaphragm. If parts are derived from the wall of the body, then it should be assumed, until proved otherwise, that nerves supplying the wall would also supply that portion of the diaphragm derived from the muscular structures of the wall. For the same reason, the phrenic nerve supplies that portion of muscular structure already described as being included within the descending diaphragm at the level of the fifth cervical segment, which is the level of its own inclusion. This implication has received attention and will be referred to again when the experimental results of phrenic neurectomy are discussed.

COMPARATIVE ANATOMY

Kingsley described the origin of the diaphragm in vertebrates, tracing its development from the fold formed by the ducts of Cuvier, which, arising in the somatopleure, enter the heart from the sides. He said:

> As they increase in diameter, they project into the coelom, carrying the somatic serosa before them. The fold thus produced is the septum transversum which is attached to the front margin of the liver. In many lower vertebrates, for example,

elasmobranches, this septum is not complete, failing to reach the other (splanchnic) wall, thus leaving one or more openings, pericardioperitoneal canals, connecting the pericardium with the body. In the higher vertebrates, the closure is complete.

In all the lung-bearing vertebrates except the mammals, the lungs are suspended in the general body cavity (splanchnocele), but in the latter group a second partition, the diaphgram, cuts off a pair of pleural cavities from the rest of the splanchnocele which is now called the peritoneal cavity.

Traces of structures similar to the diaphragm as indicated by nerve supply, and so forth, occur in vertebrates as low as the amphibia, but their exact homology is uncertain.

Comparative Anatomy of Vertebrates.—Discussing the derivation of the muscular tissue of the diaphragm, Kingsley said: "The diaphragm undergoes several shiftings of position before reaching its final place. The dorsal part of the diaphragmatic muscles is derived from the original folds, the ventral comes from the rectus abdominis muscle of the ventral abdominal wall." This makes a concrete addition to Broman's fifth division and will be referred to when the effect of phrenic neurectomy is discussed.

The study of the development of the diaphragm at different periods of fetal life introduces implications that suggest anatomic and functional probabilities. Yet there is an old method of study that may promise better results, and it is based on the obvious and well recognized fact that in the development of animal life the necessity for expanding function requires a development of organic machinery that makes function possible. This philosophy has been advanced most convincingly by Jones in his description of diaphragmatic derivations and function. It is therefore clear that when new activities and functions are contemporaneous with a new organ, the latter should be considered as responsible for the operation of the former. But functions have a tendency to develop slowly, and nature develops organs, at first simple in design and then more complex, until perfection of function is brought about by perfection in detail of the organ. Thus three pictures must be considered. When the necessity for development and for physical activities required a more efficient means of bringing oxygen to the tissue cells, the superficial layers folded in, and the first hint of a future lung was apparent. These first infoldings multiplied in number, the original lymph system became a hemolymph system, and the relationship between the circulation and respiration became established. Then the organism developed the ability rhythmically to enlarge and decrease the size of its body cavity and to produce within itself a negative pressure. Air-breathing lungs appeared and, bridging the many intermediate variables in form and design, a second picture can be visualized.

In such an animal the machinery for respiration is adequate to the needs of the animal's activities. It has lungs lying in a single celomic

cavity. They are filled and emptied by a competent three-layer musculature of the abdominal wall, but there is no evidence of a partition of the celom into two separate chambers. The stress of pressure by compression of the abdominal muscles is borne by all of the intracelomic structures equally with the lungs.

Only a rudimentary partition is present. When first observed, all rudimentary organs give a prophecy of what is to be in a new and more advanced stage of development just as vestigial organs point to a function that has passed out of the animal's economy. This rudimentary structure becomes the diaphragm of the mammals. It is well, then, to note that respiration is developed, and that the organs required are competent for all activities, activities as strenuous as those of mammals which have a perfected partition dividing the celom into two parts; however, there are observable differences.

In the lower forms the outlets of the celom are included in a single cloaca guarded by a single sphincter; in the mammals, there are multiple openings and multiple sphincters. Such an arrangement indicates, as Jones contends, an increase in intracelomic pressure. When this mechanism is complete, the diaphragm is perfected. The hint of the rudimentary structure has become the perfected organ the primary function of which must be that of increasing intracelomic pressure.

Because so many air-breathing animals have true lungs and all the muscular machinery necessary for respiration and yet do not have a diaphragm, it would be reasonable to suppose that the respiratory function was a secondary one. The diaphragm therefore can be considered as having two functions: a primary and a secondary, the latter respiratory because by rhythmic contraction the thorax is enlarged in volume, and air is brought into the lungs, the former under more direct voluntary control producing pressure so that when opposed by the abdominal musculature the sphincters can be overpowered and the products of the intestinal, the renal and the genital systems can be extruded. It is possible, as Jones has pointed out, that the change from pronograde to orthograde characteristics has modified the importance of the diaphragm as a respiratory organ and made it more essential in the latter type to which man belongs. Experimental and clinical observation, however, leads to the belief that the distinction is more theoretic than real.

This discussion does not permit of detail but rather is intended to hint at an explanation of the phenomena about to be described. Jones' article gives most comprehensively and conclusively the history of development and the functional importance of the diaphragm to animal life from the lower forms to the mammals, and he offers a theory to explain his belief in the growing importance of its secondary or respiratory function in man.

Anatomy in Man.—The anatomy of the diaphragm in man as well as in all mammals is so familiar as not to require detailed description. It is, however, important to review the opinion of anatomists and later to appraise these opinions in the light of more recent experimental evidence. LeWold has anticipated this discussion by calling attention to the fact that the diaphragm is not essential to active life in animals below the mammals. He cited the endurance and strength of the ostrich as an example of the activity possible in the absence of a diaphragm, and comparative anatomists agree that animals below the vertebrates do not have a semblance of a diaphragm, and none below the mammals has a perfected partitition. Anatomically, then, the diaphragm serves as a partition dividing the celom into its two chief chambers; it belongs to those groups of muscles which serve to enlarge and decrease the volume of the chest and which are thus important in a mechanical way for respiration. This set of muscles can be seen in action to cooperate with other groups and to act in coordination with them, and its share consists in enlarging the long diameter of the cavity of the chest. The statement found in the older textbooks on anatomy as well as in those of more recent date, that the diaphragm, next to the heart, is the most essential muscle of the body and again that it is the most important muscle of respiration, requires sober thought and perhaps modification.

ACTION OF THE DIAPHRAGM

When at rest, the diaphragm presents a domed surface due partly to the positive intra-abdominal pressure and partly to the negative intrapleural pressure. It rises higher in the thorax on the right side than on the left. During inspiration it moves downward, producing pressure on the abdominal viscera and distending the abdomen. At the same time the margins of the ribs pass outward and upward. Although the central portion moves least, the right to a greater extent, and the left through the greatest excursion, the combined movement produces an increase in the vertical diameter of the chest, and inspiration of air occurs. Although the abdominal increase in pressure during the descent of the diaphragm tends to distend the abdomen, yet, because there is opposition, the central tendon becomes a fixed point and the circumferential muscles in contraction actually elevate the lower ribs and expand the lower part of the thoracic cavity. In all acts of expulsion, sneezing, coughing, laughing, vomiting and crying, for example, the diaphragm adds power to expulsive effort.

Such was the opinion a generation ago. More recently Cunningham said: "The diaphragm, after the heart, is the most important muscle of the body. It forms the dome-shaped roof of the abdomen and the highly convex floor of the thorax." The first sentence states a belief in functional importance, the second is purely a statement of anatomic

site. The action of the diaphragm has not been affected by time or opinion, but the interpretation of its use in respiration and the conception of its correlated action with relation to the action of the intercostal and abdominal muscles have been modified.

In McLeod's description of the action of the diaphragm, he pointed out that the ascent of the ribs which increases the anteroposterior and transverse diameters of the thorax would tend to decrease the long diameter were it not for the fixation of the lower ribs and the descent of the diaphragm. Howell amplified the description by a grouping of the several muscles that bring about this result which is, in fact, the enlargement of the thorax and therefore the act of inspiration.

The vaulted dome of the diaphragm at rest, spoken of by Cunningham, is produced by the lifting action of the intrathoracic negative pressure and the upward pressure of the intra-abdominal positive pressure. Contraction of the diaphragm shortens its muscular fibers, strips off that portion lying adjacent to the thoracic walls, enlarges the volume of the thorax, increases the negative pressure and causes in its descent the phenomenon known by clinicians as Litten's sign. Gray spoke of the ability of the diaphragm actually to elevate the margins of the ribs, but McLeod explained that the attachment to the lower six ribs really tends to pull the margins toward the median line and that this tendency is overcome by the opposing action of the external intercostal muscles which raise the ribs and by the lower vertebral muscles which fix the position of the lower ribs.

The widening of the lower part of the thorax is brought about by the correlated action of groups of muscles, and before Hoover made his experimental and clinical observations, it was believed that the downward movement of the diaphragm produced the widening because it served to increase intra-abdominal pressure and the margins of the ribs were in reality forced away from the median line at the same time that the ribs were elevated, bringing about an increase of the anteroposterior and transverse diameters.

Hoover believed that the contraction of the external intercostal muscles raised the ribs and increased the angular divergence of the subcostal borders, and that the contraction of the diaphragm narrowed the subcostal angle and tended to force the margins of the ribs toward the median line. He supported the belief by observations that in paralysis of the diaphragm the subcostal angle is increased, while in paralysis of the intercostal muscles it is decreased.

These opinions are not given as expressions of fact but because they open a debatable question requiring the experimental and clinical experience of other observers. An attempt will be made to offer proof that the original belief is sound and that the descent of the diaphragm actually enlarges the outlet of the thorax and, at the same time,

increases the subcostal angle by increasing the intra-abdominal pressure. This pressure exerted on the abdominal contents, which are comparable with a fluid, becomes hydrostatic in character and is transmitted equally in all directions, forcing outward not only the abdominal wall but the margins of the ribs.

One other function needs discussion, the effect of diaphragmatic contraction on the blood pressure. Because of the increase in the intra-abdominal pressure the viscera are crowded against the inferior vena cava, blood is forced into the thorax and the immediate effect is that of raising the blood pressure temporarily. Before inspiration is complete the lessened flow tends to decrease the blood pressure. Abdominal respiration produces an initial rise succeeded by a fall in blood pressure during inspiration and an initial fall followed by a rise in pressure during expiration. These results are opposed by the effect on pressure caused by thoracic breathing in which the pressure falls and later rises during inspiration. The effect of combined breathing is the algebraic sum of these opposing influences.

Before the experimental phases of the subject are discussed, it is necessary to revert here to the sentence: "The diaphragm, after the heart, is the most important muscle of the body." I shall offer substantiation of the statement because otherwise the experimental work would lend color to the belief that the sentence is an overstatement of fact. The work best designed to influence judgment was done by Guenther and Meleney, who showed the contrast between the periodic and irregular contractions of skeletal muscles and the regular rhythmic movement of the diaphragm which is comparable with that of the heart. Like the heart muscle, the diaphragm enjoys only a brief period of rest between contractions, and the rest periods are approximately equal in length. The same remarks apply also to the other muscles regularly employed in producing inspiration and expiration. The comparison of the physiologic properties of the diaphragm with those of the extensor longus digitorum, the sartorius and the soleus convinced these authors that the diaphragm had the most efficient muscle tissue.

The diaphragm offers certain points of analogy to the muscle of the heart and in that sense partly justifies Cunningham's belief in its importance. Circulation and respiration are both fundamental and equally essential functions of the body; both are produced by muscular action, the latter only partially dependent on the diaphragm and capable of continuance without its action, the former absolutely dependent on the contraction of the heart. It may be that the diaphragm is second only in importance to the muscle of the heart but because respiration and circulation are equally essential to life, the muscular function which is dispensable suffers by comparison with that which is indispensable.

EXPERIMENTAL AND CLINICAL OBSERVATIONS

Because of the growing popularity of phrenic neurectomy in the treatment of both tuberculous and suppurative pulmonary disease, it became necessary to study the effect of such an operation on normal subjects. Study of the physiologic effect in general, as well as the respiratory mechanism, was undertaken. Healthy dogs were used in all the experiments. Later I became aware that similar work had been done on horses. Results of the study of the physiology in man could not be conclusive except in rare instances because the operation was not indicated except in cases in which the extent of involvement made it impossible to separate pathologic change from physiologic change due to the operation with consequent loss of function of at least half of the diaphragm. Suitable cases, however, have been under observation and will be discussed as they apply to the various divisions of the experimental work.

The effect of abdominal incisions and of major surgical operations on the upper part of the abdomen was studied first, because of the belief that such operation caused fixation of the diaphragm and contributed to the prevalence of postoperative pulmonary complications, which are known to be relatively much more common in cases in which the patients have been treated surgically for conditions of the stomach and gallbladder than in general surgical work. The experiments were carried out in several stages. Observations were made in the various cases studied: (1) when a simple incision in the skin constituted the surgical intervention; (2) when the abdominal wall was cut through and the abdominal cavity opened; (3) when an Eck fistula operation was performed; and (4) when an Eck fistula operation was performed and various fractions of the liver were removed. The animals were examined clinically and fluoroscopically immediately after the operation, when the animal first became conscious and every succeeding day until the wound was healed. In none of the animals was any fixation of the diaphragm discovered. The excursion was normal and equal to that before operation. I have never seen an animal under any of these conditions with restriction of diaphragmatic movement.

This observation is not reported in an iconoclastic spirit. It has to do with an animal and not with man. I do not know whether it is a true statement in regard to the diaphragmatic movement in man under similar circumstances. No one, to my knowledge, has made any such experimental study on man. The reports have been based on purely clinical examination and are therefore subject to personal error. No one can reproduce in a dog the conditions found in man: the debility that called for the necessity of operation, the anxiety and apprehension before and after operation, and the acuteness of sensibility to pain that

lowered vital capacity and slowed the venous stream within the abdominal veins. My impression is, however, that the abolition of the resistance of the abdominal musculature against the downward thrust of the diaphragm has more to do with postoperative conditions than has been supposed. There are other considerations. The dog does not lie on his back; he is not trussed up with dressings, adhesive bandages and encircling binders that compress the margins of the ribs and prevent movement at the bases of the lungs where movement is most necessary to prevent congestion. With a slowed venous stream and a congested lung, both infarct and infection become not only possible but even probable. The low vital capacity in man is more an expression of abdominal pain preventing resistance to diaphragmatic contraction than to any loss of power in the efficiency of the diaphragm itself.

UNILATERAL PHRENIC NEURECTOMY

When evulsion of the phrenic nerve is carried out, half of the diaphragm is promptly paralyzed. Atrophy starts as early as the second day, and is manifested grossly by pallor and edema in both dog and man. The diaphragm rises in the thorax and does not take any further part in respiration. It either is immobile or takes on paradoxic movement due to the alteration in intra-abdominal pressure that is produced by contraction of the unaffected portion. The only difference between the dog and man lies in the higher elevation of the vault of the paralyzed hemidiaphragm in man. I have noticed this in examining all of my animals and comparing them with the human subjects on whom unilateral phrenicotomy had been performed for various reasons, as well as those rather rare cases of true eventration of the diaphragm. It has seemed to me that the cause was to be found in the difference between the pronograde and the orthograde animal and in the purely carnivorous and the partly carnivorous types. The relatively small abdominal content in the carnivorous group fails to elevate the paralyzed portion to the same degree.

The movements of the thoracic wall have been studied both in animals and in man. Kymographic records have been made to check inspection, but in every instance the movements of the chest as a whole and of its several parts have remained unchanged. It was expected that the movement of the costal margin would be increased on the side affected, but this could not be substantiated in my experiments. I have been unable to convince myself by any means at my disposal that such a phenomenon is present in man, and I have examined patients repeatedly for days after phrenic neurectomy, patients with eventration and a single patient who was shown at operation to have congenital absence of half of the diaphragm. Lord, in discussing cases

of eventration, spoke of the symmetry of the chest, but in one case he noted a difference of 1 cm. in the circumference of the two sides and an increased excursion of the whole chest from the left clavicle to the costal margin. There was exaggeration of the inspiratory widening of the subcostal angle and costal margin of the affected side and an inspiratory retraction of the epigastrium. In another case in which the dome of the left side of the diaphragm was shown opposite the anterior portion of the first rib, he noted again the symmetry of the chest; the left circumference was 0.5 cm. greater than the right, and the expansion of the two sides of the chest as a whole was the same, but there was exaggerated divergence of the left costal margin from the median line in the epigastrium with consequent greater widening of the left than of the right side of the subcostal angle.

I have been unable to convince myself by the observation of five patients that the costal margin is permitted a greater latitude of movement because of paralysis of the hemidiaphragm on that side. On one patient observed recently phrenic neurectomy had been performed a year previously. The chest was symmetric and the movements, by inspection, appeared to be the same on the two sides. When readings were made with the kymograph, the costal margins and the costal arch showed a greater latitude of movement over the affected side than on the normal side. This is the only case that has given such a record. I have not seen any difference in animals on examination, in measurements of lateral movement or from the study of kinematographic records. Moreover, before killing the animal by overetherization, I have stripped the skin and superficial tissues free from the epigastrium and from the costal arches and have been unable to see differences in the degree of movement on the two sides. It is reasonable to expect that the muscular layers of the chest should oppose the movement of the diaphragm because they should behave like the muscles of the abdomen. I have no doubt of the accuracy of the observations of Hoover and Lord or of those of Funk and Manges, Korns or Reifenstein, but I do not believe that the phenomena they describe are always present, and I am convinced that they are not in a pronograde animal such as the dog.

The dogs could perform any ordinary activity without respiratory distress and did not seem to show evidence of lowered vital capacity. Even those in which the whole diaphragm was paralyzed by bilateral phrenic neurectomy ran and played like normal animals and after exercise could not be separated from normal dogs by those who were not acquainted with them.

In the case of one patient, evulsion of the left phrenic nerve was carried out because of a small localized area of bronchiectasis. There

was reduction in vital capacity of approximately 20 per cent, but within nine days the capacity reading was normal. In another case, left phrenic neurectomy was done because of localized bronchiectasis, and symptomatic cure resulted. The patient does her housework without respiratory embarrassment, and she is not troubled with dyspnea or gastric distress. Cough is infrequent, and more effectual in raising sputum than before operation. The vital capacity reading is 3,403 cc. The estimated normal reading would be 3,050 cc. The removal of 8 cm. of the phrenic nerve paralyzed the left side of the diaphragm which rose high in the thorax and was immobile on both general and fluoroscopic examination. The left side of the chest measured 38.5 cm. and the right 39 cm., a difference so small that it may be explained as a personal error or may represent what could be called normal asymmetry of the chest. Differences in the movement of the chest could not be observed by inspection, by combined inspection and palpation or by actual measurement during inspiration or when at rest. These observations were checked by observers who were not acquainted with the patient's history and were entirely disinterested and unprejudiced.

Three other patients were dyspneic on exertion, but other complications were present that may have been responsible for the dyspnea. Welles did not observe any evidence of undue shortness of breath or any abdominal disturbances after the operation in forty-nine of fifty cases of unilateral phrenicotomy. Yeates performed eighteen radical operations of extraction or resection and reported that none of the intra-abdominal functional disturbances could be attributed to the paralysis. "Paralysis of the diaphragm reduces vital capacity, restricts external respiration and impairs competence. Dyspnea on exertion is inevitable." Experimental evidence permits certain definite conclusions: 1. A dog can live comfortably without diaphragmatic movement. 2. He can live for many days following transection of the spinal cord between the sixth and seventh cervical vertebrae so that the diaphragm is almost totally responsible for respiration. 3. He can still live even after transection of the cord and evulsion of one phrenic nerve.

Conversely, clinical evidence permits the conclusion that a man can live after a low fracture of the neck has paralyzed thoracic and abdominal muscles and the diaphragm is almost entirely responsible for respiration. I have examined three such patients living almost entirely from diaphragmatic movement. The chest as a whole retracted with inspiration and the consequent increased negativity of intrapleural pressure, but the costal arches and margins moved outward because of the increased positive pressure due to the descent of the contracting diaphragm.

It was formerly said that man, unlike a dog, cannot live if he loses diaphragmatic function. I have not examined a case in which there was

bilateral phrenic paralysis. Jones said that the primitive (pronograde) mammal is dependent on the external respiratory system, while man has become dependent on the internal respiratory system. He believed this dependency to be due to the loss of fixation of the fore limb and shoulder girdle. This hypothesis, however, is no longer accepted. It is well known that man can live not only with half of the diaphragm paralyzed, but also with the whole diaphragm rendered functionless. Cases reported by Gamble, Pepper and Mueller and also by Dowman confirm this belief.

EXPERIMENTS ON ASPIRATION

Because of the importance of aspiration of secretions into deep portions of the bronchial tree, thereby adding to the total amount of infected lung, it became necessary to determine whether there was sufficient suction during inspiration to cause such aspiration in an animal the hemidiaphragm of which is paralyzed. This is an important consideration in both tuberculous and chronic suppurative conditions in both of which infection may be spread by aspiration. Accordingly, an animal with half of the diaphragm completely paralyzed was anesthetized with ether for twenty minutes during which time 40 per cent iodized oil was slowly introduced into the trachea. Ten minutes later he was killed by overetherization, the trachea being clamped to maintain expansion of the lungs. The lungs were examined fluoroscopically and oil was seen to have been aspirated into both lungs, showing that the paralyzed diaphragm did not affect inspiratory suction sufficiently to prevent the aspiration of intratracheal material. One cannot hope that in such diseases as tuberculosis and bronchiectasis the lungs will be spared from the risk of aspiration.

NECROPSY REPORT

The examination of dogs at necropsy did not show evidence of abnormality in the heart, pericardium, pleura or lungs. Evidence was lacking of congestion or other impairment in the circulation of blood through the lungs. Brown's later work confirmed the conclusions reached from my gross and microscopic data, although his method of study was entirely different. My own observations have been repeated many times, and the conclusions have remained unchanged. Thus far I have not been able to produce evidence that the diaphragm has a double motor innervation, although the embryologic development might lead one to suspect that nerves supplying the muscles of the body wall might also supply that portion of the diaphragm which is derived from them. Higgins has discovered that the thirteenth thoracic nerve in the dog sends fibers to the diaphragm, but there is no assurance that this is motor in function.

CONCLUSIONS

It would appear from the study of comparative anatomy that structures similar to the diaphragm play varying parts in respiration, acting as expiratory, as inspiratory and at other times as both expiratory and inspiratory organs. Without doubt higher forms of animals, possessing true lungs and equipped with musculature which provides efficient respiration, breathe without the aid of a diaphragm. It is likewise true that a perfected diaphragm coincides with a mechanism developed to support high intracelomic pressure. All of these facts lead one to believe that the providing of pressure is the chief and primary function of the diaphragm and that its purpose as a partition is to allow the increased pressure to act on abdominal viscera, permitting them to discharge their contents (fecal matter, urine and offspring), while at the same time the heart and lungs are spared the effects of the same pressure. It would appear that animals such as the dog can maintain respiratory efficiency without impairment when half of the diaphragm has been paralyzed and even when both sides are functionless and, in fact, a hindrance to respiration. In such animals the diaphragm does not compare in functional importance with the heart. Man can live comfortably when half the diaphragm is paralyzed, and he suffers only a slight loss in vital capacity. It seems probable that this loss is quickly made up by factors of compensation.

Alexander stated: "Phrenectomy has not been known to cause dyspnea or other respiratory disturbance. In fact, Jehn, Sauerbruch, Lehman, Dehler and Stern have performed bilateral phrenicotomy for persistent singultus, or to permit artificial respiration in diaphragmatic tetanus, and have not seen noteworthy respiratory disturbance. Jehn's patient led an active life three and a half years after the operation and was never dyspneic."

This report is later than that of Jones who reported Bell's case of bilateral phrenic paralysis, which resulted fatally. It seems probable that the patient may have suffered paralysis of the thoracic musculature as well, because the cervical vertebrae were fractured. The fractures of the neck, I have observed, were all below the level of the origin of the phrenic nerve, and I have not had any personal experience with operations on both phrenic nerves.

The experiences of other observers are more conclusive than mine in regard to the opposition of the thoracic musculature to the movement of the diaphragm. It seems certain that this is the function of the abdominal muscles in relation to primary diaphragmatic function of increasing intracelomic pressure and from analogy should be true of the thoracic group. Certainly the increased subcostal angle and the

increased movement of the costal margin have been too uncertain to constitute a dependable test of diaphragmatic elevation, depression or function.

Unilateral diaphragmatic paralysis provides rest for a diseased lung and produces functional benefit in disease, but it does not protect against spread of the disease by aspiration of bronchial or tracheal contents. Contrary to my expectation, but in agreement with Schloepfer, I found that the phrenic nerve was the only demonstrable motor nerve to the diaphragm. Felix believed that the twelfth intercostal nerve supplied motor innervation to the few fibers arising from the level of the twelfth rib. The paralysis I observed in dogs was so prompt and so complete that I suggested the importance of phrenic neurectomy as an adjunct to precede operations in the upper part of the abdomen of patients when the movements of contraction were a hindrance to success. Harrington adopted the method and has used it successfully in the surgical treatment of diaphragmatic hernia, and for the cure of thoracic tumors involving the diaphragm. It is probable that respiration is maintained as a result of a mechanical process operated by the combined movements of various sets of muscles so coordinated and controlled as to make possible an exchange of air sufficient not only at rest but also under effort. It seems probable that groups of muscles can be rendered functionless without disturbance of respiration as a whole or the action of other groups separately. The loss in vital capacity varies with the degree of muscular dysfunction.

THE SURGICAL SIGNIFICANCE OF THE ABDOMINAL REFLEXES *

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The diagnosis of acute intra-abdominal diseases has taxed the ability of the internist, pediatrician and surgeon alike. The literature on the subject is voluminous, but most writers have not stressed the signs which do not require the assistance of the laboratory. Any symptom that can be elicited at the bedside is a welcome aid to the diagnostic armamentarium.

The cutaneous abdominal reflexes have not received their proper place as a valuable aid in the diagnosis of acute intra-abdominal disease. The literature on this topic is scant. Most writers have dealt with hyperesthesia, but the contraction reflex has been singularly omitted. Smith [1] is an outstanding exception. The neurologists, such as Monrad-Krohn [2] and others, spoke of abdominal reflexes and did not include hyperesthesia, whereas, surgeons, such as Robinson,[3] Logat [4] and Cope,[5] captioned their articles abdominal reflexes and described hyperesthesia of the skin, but failed to mention the contraction reflex. Both are important and may be significant in the same pathologic condition. It is essential, therefore, to bear in mind that hyperesthesia and the contraction reflex are not the same.

Hyperesthesia may be defined as a response to a stimulus expressed in terms of pain. It is, in reality, a form of hyperalgesia, as is all abdominal tenderness due to visceral inflammation. Its interpretation is dependent on the patient's statement and cooperation. It becomes evident that this reflex pain cannot be controlled by the patient. It is not definitely known how this increased pain over an inflamed abdominal organ is produced. Livingston [6] believed that it is caused by the transmission of the painful sensation by the visceral nerves through the nervi communicanti to the spinal nerves and so to the overlying skin.

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* Read before the Bronx Surgical Society, April 25, 1928.

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2. Monrad-Krohn, G. H.: Norsk Mag. f. Laegevidensk., Dec., 1918, suppl. vol. 79.
3. Robinson, H.: Quart. J. Med. **1**:387, 1908.
4. Logat, D.: Lancet **1**:724, 1919.
5. Cope, Z.: The Early Diagnosis of the Acute Abdomen, New York, Oxford University Press, 1924.
6. Livingston, E. M.: Further Study of Viscero-Sensory Phenomenon, J. A. M. A. **82**:1495 (May 10) 1924.

The cutaneous contraction reflex can be defined as a response to a stimulus expressed in terms of involuntary muscular contraction, usually not accompanied by pain. Here the element of correct interpretation is independent of the patient's statement or intelligent cooperation. It is, therefore, of inestimable value in children.

The paths and mechanism of this contraction reflex is not definitely known. Many neurologists believe that they are cerebral, while others think that the complete cycle is in the spinal cord. Whether one or the other view is correct, it seems to me that other factors enter into its mode of production and repression.

The anterior abdominal wall is supplied by the lower seven intercostal nerves, which carry the motor and sensory fibers. The muscles of the abdominal wall are of the voluntary group and can be contracted and relaxed at will. Normally, one either contracts or relaxes the whole anterior abdominal wall, but does not have control over any particular segment. The cutaneous reflexes, whether hyperesthesia or muscular contraction, differ in that they are unilateral and segmental. The hyperalgesia cannot be controlled by the patient, that is, the pain is present whether the patient says so or not. The contraction reflex can be controlled by voluntarily holding the muscles in a state of tension. Experimentally, it was shown that when the cutaneous nerves are severed, the muscular tone is still maintained, but the reflexes are abolished. The fact that the voluntary control of the abdominal muscles is synchronous on both sides while the normal reflexes are unilateral and segmental is more evidence that the muscular control and the cutaneous reflexes have different centers. It therefore seems logical to conclude that the cutaneous reflexes are spinal, but that the muscular control is elsewhere, probably in the cerebral system. As will be shown later, there may be rigidity of the abdominal muscles with the reflexes exaggerated, diminished or absent, depending on the underlying cause of the rigidity.

GENERAL CONSIDERATIONS

The cutaneous abdominal reflexes are absent in the first six months of extra-uterine life. They become active in the second half of the first year, and their presence at this age can be elicited with difficulty. From then on they differ in their activity and are not to be interpreted in the same way.

Hyperesthesia consists of a sensation of increased pain when the skin over a particular area is pinched. Only the skin must be stimulated, and not the underlying tissues. It is present in the early stages of disease of an intra-abdominal organ. The pathologic condition must not necessarily be an acute inflammation. Any process that causes increased tension, increased peristalsis or acute inflammation will give hyperalgesia. It

must be remembered that pain is a relative term, and can be interpreted only by comparing both sides of a particular segment. It is of much value in the adult, but cannot be relied on in children, as the young will mislead when asked which side is more sensitive. This capacity for hyperesthesia in disease persists till late in life, and can be extremely active from adolescence till about 50 years of age. From then on it diminishes, and it is of little value in old people. This reflex is present early in the pathologic process. When the inflammation progresses and the peritoneum becomes involved, it diminishes in intensity and is finally lost in the late stages of peritonitis. At this stage, the contraction reflex is of value, as will be shown later.

The cutaneous contraction reflex is produced by scratching the skin with a sharp, pointed object, such as a pin or a sharp pencil. It is seen as a homolateral, segmental contraction of the muscular segment at the site of stimulation. The linea alba and the umbilicus deviate to the same side. This contraction occurs almost simultaneously. A heterolateral contraction is pathologic and usually belongs to diseases of the spinal cord, such as poliomyelitis.

After the first six months of life, this reflex is extremely active and can be elicited in the young. It persists actively in the young and diminishes in importance in the older person. The retrogression is not alike in both sexes. It persists longer in the male and is at times seen late in life. In the female, it tends to diminish with the advance of adiposity and the relaxation of the abdominal wall consequent on child bearing. These patients retain part of their contraction reflex in the upper part of the abdominal muscles which overlie the lower costal cartilages; here the amount of fat is scant, and the striae due to stretching of the muscles are absent. It is interesting to note that the abdominal wall of obese males retains the contraction reflex longer than a similar abdominal wall in the female.

From the foregoing considerations, it becomes evident that the hyperesthesia is of value in the adult while the contraction reflex is of inestimable value in children.

For convenience, the abdominal wall may be divided into four parts: upper right and left and lower right and left. Some neurologists speak of gastric, umbilical and midabdominal areas, but for the practical purposes of the surgeon, the division into four parts is sufficient.

In eliciting the contraction reflex, the pointed instrument should be almost perpendicular to the skin. In the upper segments of the abdomen, the motion should be from above downward. Beginning at about the tenth costal cartilage just lateral to the nipple line, the stroke is directed downward for about 8 cm. In the lower parts the scratch is lateral, beginning away from the median line and directed inward. The linea alba must not be crossed.

The cremasteric reflex cannot properly be called an abdominal reflex, as the cremasteric muscle is supplied by the external spermatic branch of the genitofemoral nerve. This reflex can be elicited in the triangle formed by a line drawn from the middle of Poupart's ligament inward and meeting the sartorius muscle which forms the inner boundary of the triangle. This reflex is exaggerated in cases of ureteral colic or other diseases of the urinary tract and remains unaffected by intra-abdominal pathologic changes. It is, therefore, of great help in distinguishing ureteral colic from acute appendicitis.

I have studied 200 cases with relation to these reflexes. Special attention was paid to the contraction reflex as this, to my mind, is the more important of the two. Besides, the hyperesthesia reflex is present in only about 50 per cent of the acute cases in adults, in which cases the diagnosis is not as difficult.

As a general statement, it can be said that whenever the anterior parietal peritoneum becomes involved in an acute inflammatory process, the cutaneous contraction reflexes are abolished. The degree of suppression is in direct ratio to the severity of the pathologic process. The area of absence of this reflex overlies the diseased organ. When the peritonitis is diffuse; the whole abdominal wall is nonresponsive. In well localized inflammatory processes, such as appendicitis and pericholecystitis and others, the overlying area of skin does not respond to the scratch. The immediately surrounding areas show a diminution of this reflex and the opposite side responds normally.

In children, in whom it is often difficult to differentiate between intrathoracic lesions and an acute surgical condition of the abdomen, I find that in the former condition the abdominal contraction reflex is present and exaggerated while in the latter this reflex is abolished. This is well illustrated in the following case.

REPORT OF CASES

CASE 1.—J. Lubell, aged 4 years, had a past history that was irrelevant. The child began to complain of pain in the abdomen at 7 p. m.; he vomited soon afterward. This pain continued intermittently all night. I saw the child with Dr. Blutstein at about 10 a. m.; at this examination, the child looked ill. The temperature was 103 F. and the abdomen was tense, but a satisfactory examination could not be made as the child cried continually. Repeated enemas since the previous night were not of avail. Examination of the chest did not reveal any definite signs of a pulmonary lesion. The abdomen was distended, and the contraction reflexes were somewhat exaggerated; this ruled out peritonitis. The diagnosis of pneumonia was confirmed thirty-six hours later. The child recovered.

In cases of intussusception or other forms of intestinal obstruction, the contraction reflexes are present at first but diminish later. When gangrene sets in or the transudate becomes toxic, the reflex is abolished.

When the reflexes are absent early, the condition is indicative of a marked peritoneal involvement, and immediate interference is imperative. The following case illustrates this fact.

Case 2.—M. Scoglio, a girl, aged 11 years, had been operated on by me for an acute appendicitis on Feb. 2, 1928. The abdomen was drained for a few days. At that time, I noticed that the gallbladder was much enlarged. In the presence of infection, I refrained from doing anything to this organ. The patient was discharged on February 19, cured. On March 11, she began to complain of pain in the abdomen, mostly on the right side. Vomiting began soon afterward and continued for eight hours. When I saw her in consultation with Dr. Astrachan, the temperature was 101 F., the pulse rate 98 and the respirations 26. The abdomen was distended and extremely tender throughout. The abdominal reflexes were absent. In view of the previous laparotomy, a tentative diagnosis of intestinal obstruction was made. As the reflexes were absent, peritonitis was thought of, but was mentioned only as a probability. On making an incision into the abdomen, I found a ruptured gallbladder. This well illustrated that the absence of the reflexes was too early for an intestinal obstruction, but indicated peritonitis.

In cases of fulminating peritonitis, such as pneumococcus or streptococcus forms, the reflexes are absent early and throughout the entire abdominal wall. In hemic peritonitis, the contraction reflexes are present at first, but tend to diminish later as absorption from the peritoneal cavity takes place. This is of some significance in children but not in adults. In cases of rupture in ectopic pregnancy, it is generally of less value as these patients are often obese and frequently multiparae.

Cases of ruptured appendixes occur in which the contraction reflex is only diminished. In these, the appendix is retrocecal, and the toxic material has not invaded the anterior parietal peritoneum. The process, however, soon extends and the anterior wall becomes involved. The reflexes are then abolished.

It must not be concluded that all forms of abdominal rigidity show an absence of this reflex. When the rigidity is the result of a general involvement of the nervous system, as for instance, meningitis, the abdomen may be rigid and the reflexes markedly exaggerated. This is well illustrated in the following case:

Case 3.—H. M., aged 22, a drug clerk, while carrying a ladder, had felt a severe pain over the abdominal wall. It soon radiated to the back and was followed by a mild chill. Two hours later, he vomited twice, and the pain in the abdomen increased. Two enemas were ineffectual. I saw him twelve hours later. Examination revealed a rigid abdomen, with tenderness more marked on the right side. The patient could not retain anything taken by mouth and appeared ill; the temperature was 101 F., the pulse rate 90 and the respirations 26. The contraction reflexes were exaggerated, and the spine was somewhat rigid. The condition proved to be meningitis. The exaggerated reflexes drew my attention to the spine. I confess that if it had not been for the reflex phenomenon, this patient might have undergone a laparotomy.

CONCLUSIONS

1. The cutaneous abdominal responses are of two kinds: (1) hyperesthesia, which is increased pain when the skin is pinched over a diseased organ, and (2) the contraction reflex, which is a response to scratching of the skin over a particular area.

2. Hyperesthesia is of value in diagnosing conditions in adults, while the contraction reflex is helpful in diagnosing disease in young persons.

3. Hyperesthesia is present early in the course of abdominal disease (in about 50 per cent only) and diminishes later. The contraction reflexes are absent when the peritoneum becomes involved.

4. Both reflexes are unilateral and segmental.

5. Rigidity of the abdominal wall, not the result of an intra-abdominal condition, may be accompanied by an exaggerated contraction reflex, while that caused by inflammation of the peritoneum results in the absence of this reflex.

6. In the obese and multiparas, the absence of the contraction reflexes is not of any particular significance, but the hyperesthesia has definite value.

RELATION OF BACILLUS WELCHII ANTITOXIN TO THE TOXEMIA OF INTESTINAL OBSTRUCTION

EXPERIMENTAL STUDIES *

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It is now generally recognized that death in cases of intestinal obstruction is due to the establishment of a toxemia. Two main theories have been advocated to account for the formation of the toxin concerned. One group of investigators [1] believes that the toxin is elaborated by a perversion of function of the mucosa cells lining the obstructed loop; the other group [2] assumes that the bacterial flora within the loop is responsible. The weight of experimental evidence to date is difficult to evaluate, but a communication by William [3] demands that we investigate a known bacterial toxin which may possibly have a bearing on the problem. Williams thinks that the toxemia results from the absorption of *Bacillus welchii* toxin. He gives evidence of the proliferation of the organism in the small bowel in cases of obstruction, and likewise of the presence of the toxin by the injection of the loop filtrate into mice; however, he has been unable to show that this toxin is absorbed. In a recent publication, Scholefield [4] concludes that the toxemia is due to the absorption of a toxin through the portal circulation.

EXPERIMENTAL WORK

The following experiments were undertaken to test the validity of Williams' observations. A standard experiment was used throughout, the conditions being maintained as nearly constant as possible. In dogs that were not fed the day

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2. Murphy, F. T., and Vincent, Beth: The Cause of Death in Intestinal Obstruction, Boston M. & S. J. **165**:684, 1911. Murphy, F. T., and Brooks, B.: Intestinal Obstruction, Arch. Int. Med. **15**:392 (March) 1915. Dragstedt, L. R.; Moorhead, J. J., and Burcky, F. W.: Intoxication of Closed Intestinal Loops, J. Exper. Med. **25**:421, 1917. Dragstedt, L. R.; Dragstedt, C. A.; McClintock, J. T., and Chase, C. S.: Extirpation of the Duodenum, Am. J. Physiol. **46**:584, 1918. Dragstedt, C. A., Cannon, P. R., and Dragstedt, L. R.: Effect of Acute Obstruction and Stasis on Bacterial Types, J. Infect. Dis. **31**:209, 1922.

3. Williams, B. W.: Toxemia of Intestinal Obstruction, Brit. J. Surg. **14**:295, 1926.

4. Schoelfield, B. G.: Acute Intestinal Obstruction, Guy's Hosp. Rep. **77**:160, 1927.

before operation, obstructions were produced by dividing the jejunum and inverting the ends at a measured distance (10 inches) below Treitz's ligament.[5] Ether anesthesia was employed. Water was allowed when desired following operation, but nothing else was given by mouth. The nonprotein nitrogen and blood chlorides were determined before and every day after the operation, specimens being taken from the jugular vein each morning. The nonprotein nitrogen of the whole blood was determined by the method of Folin and Wu, and the chlorides by a modification of the method of van Slyke. The degree of toxemia was judged from the clinical appearance of the animal and by the increase in the nonprotein nitrogen of the blood. It is not possible to estimate any exact day on which the toxemia will occur, as great variation takes place in this regard. When the dog appeared definitely toxic, and when the nonprotein nitrogen was over 40 mg. per hundred cubic centimeters, the various procedures outlined subsequently

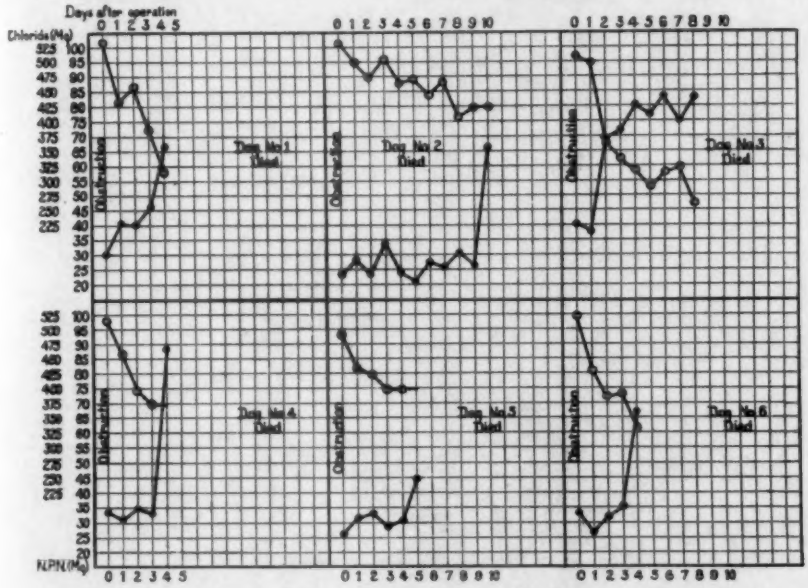

Chart 1.—Results of obstruction of the jejunum in untreated dogs.

were carried out. Operations were invariably performed with the dog under ether anesthesia, and neither fluid nor salt solution was given to the animals, special care being taken to avoid saline on account of the beneficial effects shown by Haden and Orr.[6] The test was made difficult purposely, and it is realized that possibly better results could have been obtained by using local anesthesia, forcing fluids and bringing the salt balance back to normal. In all cases milk was allowed after the release of an obstruction by lateral anastomosis between the loops.

Obstructions were produced by dividing the jejunum and turning in the ends 10 inches below Treitz's ligament. Death occurred in from four to ten days with a rise in the nonprotein nitrogen and a fall in the blood chlorides. This served as the control series (chart 1, table 1). This group does not differ in any

5. The suspensory ligament which marks the transition between the duodenum and the jejunum is referred to as Treitz's ligament throughout this communication.

6. Haden, R. L., and Orr, T. G.: Obstruction of the Jejunum, Arch. Surg. **11**:859 (Dec.) 1925.

essentials from that observed by other investigators. It corresponds well with Haden and Orr's control series.[6] Most of the animals died in from three to four days with a rapid rise in nonprotein nitrogen. Occasionally, an animal failed to develop toxemia and the blood chemistry remained practically normal for over a week (dogs 2 and 3). The case of dog 3 is especially interesting in that the nonprotein nitrogen started at a high level and remained there for so long a time without toxic symptoms. The kidneys of this animal, however, showed chronic nephritis, which probably accounted for the observations.

TABLE 1.—*Obstruction of the Jejunum in Untreated Dogs*

		Blood, Amount per 100 Cc.		
Dog No.	Day after Operation	Total Nonprotein Nitrogen, Mg.	Chlorides, Mg.	Comment
1	0	30.0	531	Obstruction
	1	40.7	435	
	2	40.2	456	
	3	45.8	386	
	4	66.6	315	Died
2	0	23.1	531	Obstruction
	1	28.2	498	
	2	23.0	473	
	3	33.5	502	
	4	23.8	461	
	5	20.8	468	
	6	27.1	444	
	7	25.5	465	
	8	30.4	405	
	9	26.0	423	
	10	65.0	424	Died
3	0	40.0	508	Obstruction
	1	37.5	498	
	2	68.4	360	
	3	71.5	335	
	4	80.0	316	
	5	76.9	286	
	6	83.0	312	
	7	75.0	321	
	8	82.2	260	Died
4	0	33.3	515	Obstruction
	1	30.8	457	
	2	34.5	396	
	3	32.6	378	
	4	88.2	...	Died
5	0	25.4	490	Obstruction
	1	31.6	433	
	2	33.3	422	
	3	28.6	398	
	4	30.8	397	
	5	44.8	...	Died
6	0	33.1	522	Obstruction
	1	26.8	428	
	2	31.6	386	
	3	35.5	390	
	4	67.0	332	Died

Obstruction at the same point was produced in second group of six dogs. After the toxemia was well established, as evidenced by the clinical appearance and blood chemistry, a lateral anastomosis was performed between the obstructed loop and the collapsed bowel below it (chart 2, table 2). Five of the six animals so treated died as a result of the toxemia and operation. The sixth animal was not really toxic when the obstruction was released. The toxicity developed so rapidly in some of the animals that anastomosis could not offer much chance of survival (dogs 9 and 11). Dogs 10, 12 and 13, however, had a good chance of recovery. In general, it seems fair to conclude that when the toxemia has become well established, surgical procedure alone will not effect a cure. The chances can be much

improved by local anesthesia, hypodermoclysis, increase in the sodium chloride and possibly by emptying the obstructed loop of its contents or removing the distention (enterostomy).

Two dogs were given *B. welchii* antitoxin intravenously, the amount being based on 1.5 cc. serum per kilogram of body weight. After this, the bowel was obstructed (chart 3, table 3). Both dogs were slow in developing toxemia and died only after eleven and fourteen days, respectively. The antitoxin seemed to delay the toxic symptoms. Additional experiments of this kind must be carried out.

Eleven dogs were given *B. welchii* antitoxin intravenously and obstructions produced as previously described. After a toxemia was well established, a lateral

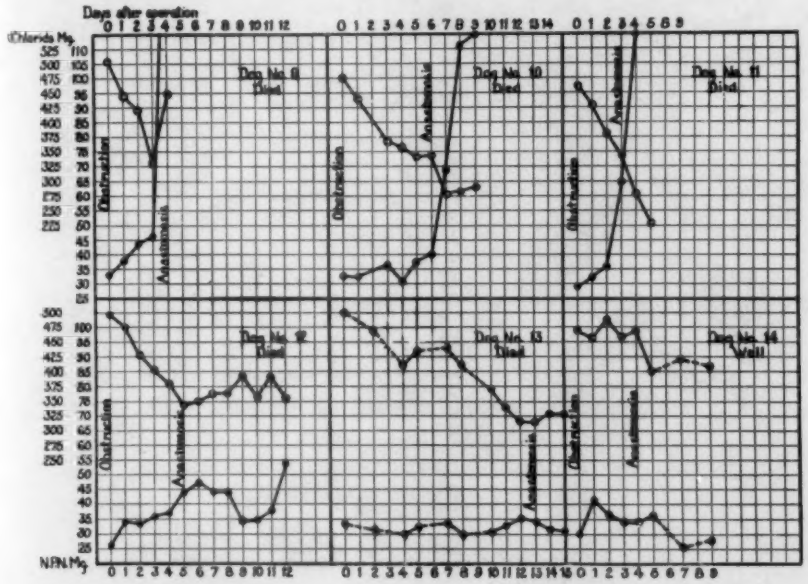

Chart 2.—Results of obstruction of the jejunum with lateral anastomosis after toxemia had been established.

anastomosis was performed to relieve the obstruction, and more *B. welchii* antitoxin was administered (chart 4, table 4). Eight of the eleven animals survived the toxemia and operation and recovered; three animals died. Animals 15, 16, 17 and 18 were treated with a dilute antitoxin, and the results were uniformly successful. After this, the manufacturing company stopped making the dilute antitoxin and supplied only a "concentrated" form. This was the antitoxin used on animals 19, 20, 21 and 22, only one recovering. Whether the concentration of the antitoxin produced this change in the results is not known. Animals 29, 30 and 31 were given the unconcentrated form of the original successful serum, but the unit value was double that of the former. It is the impression that the dogs treated with *B. welchii* antitoxin develop toxemia more slowly after the obstructions are established and that the same animals withstand operation better than normal dogs with obstructions. Haden and Orr[9] showed that when toxemia had been

TABLE 2.—*Obstruction of the Jejunum with Lateral Anastomosis After Toxemia Was Established*

Dog No.	Day after Operation	Blood, Amount per 100 Cc.		Comment
		Total Nonprotein Nitrogen, Mg.	Chlorides, Mg.	
9	0	33.3	504	Obstruction
	1	38.2	445	
	2	42.9	421	
	3	46.2	328	
	4	162.0	350	Lateral anastomosis
10	0	32.8	475	Obstruction
	1	32.6	440	
	2	....	...	
	3	36.7	369	
	4	31.5	356	
	5	37.5	344	
	6	40.0	344	Lateral anastomosis
	7	69.0	277	
	8	111.0	285	
	9	115.0	289	Died
11	0	29.0	402	Obstruction
	1	32.0	427	
	2	35.2	379	
	3	65.0	344	Lateral anastomosis
	4	115.0	280	
	5	207.0	230	Died
12	0	25.9	498	Obstruction
	1	34.2	475	
	2	33.7	427	
	3	36.1	404	
	4	37.5	379	
	5	44.5	344	Lateral anastomosis
	6	47.2	350	
	7	43.7	361	
	8	43.8	362	
	9	34.0	391	
	10	35.0	356	
	11	38.0	391	
	12	54.6	356	Died
13	0	33.3	500	Obstruction
	1	....	...	
	2	31.6	470	
	3	....	...	
	4	30.0	410	
	5	32.6	433	
	6	....	...	
	7	33.3	440	
	8	30.0	410	
	9	....	...	
	10	30.7	370	
	11	33.0	340	
	12	35.3	316	
	13	34.3	314	Lateral anastomosis
	14	31.6	328	
	15	31.0	328	Died
14	0	30.2	468	Obstruction
	1	41.4	457	
	2	36.3	487	
	3	34.5	457	
	4	34.3	468	Lateral anastomosis
	5	36.4	400	
	6	....	...	
	7	25.9	422	
	8	....	...	
	9	28.2	410	Well

established in an animal with intestinal obstruction, administration of sodium chloride would combat the toxin and put the animal in condition to withstand an operation for relief from the obstruction. It seems that *B. welchii* antitoxin also has some value in this respect, 72.7 per cent of the animals having recovered. The antitoxin was given before the obstruction was produced, because it was considered that a slight effect of the antitoxin could be better observed. It was not certain how potent this antitoxin would be in its action if the toxemia had become well established. It was, therefore, regarded much the same as the tetanus antitoxin which is known to be effective as a prophylactic agent against tetanus toxin but much less useful when the disease is present.

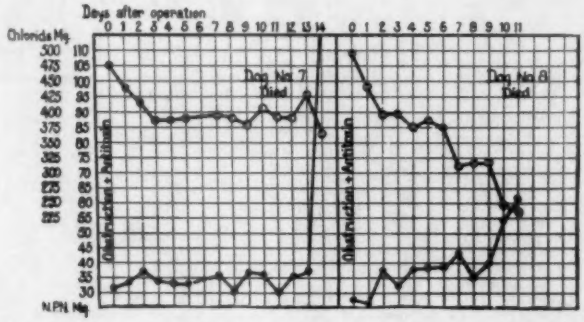

Chart 3.—Results of obstruction of the jejunum followed by administration of *B. welchii* antitoxin.

TABLE 3.—*Obstruction of the Jejunum with Administration of B. Welchii (Perfringens) Antitoxin*

		Blood, Amount per 100 Cc.		
Dog No.	Day after Operation	Total Nonprotein Nitrogen, Mg.	Chlorides, Mg.	Comment
7	0	31.6	475	Obstruction and antitoxin
	1	33.3	438	
	2	36.3	415	
	3	33.3	385	
	4	32.4	385	
	5	32.5	390	
	6	....	...	
	7	35.3	396	
	8	31.6	390	
	9	36.5	380	
	10	35.9	405	
	11	30.2	392	
	12	35.3	390	
	13	37.5	427	
	14	120.0	362	Dead
8	0	28.7	495	Obstruction and antitoxin
	1	29.1	440	
	2	37.3	398	
	3	33.0	398	
	4	37.5	375	
	5	38.7	396	
	6	37.1	375	
	7	43.8	310	
	8	35.5	316	
	9	40.0	316	
	10	54.5	246	
	11	62.6	234	Died

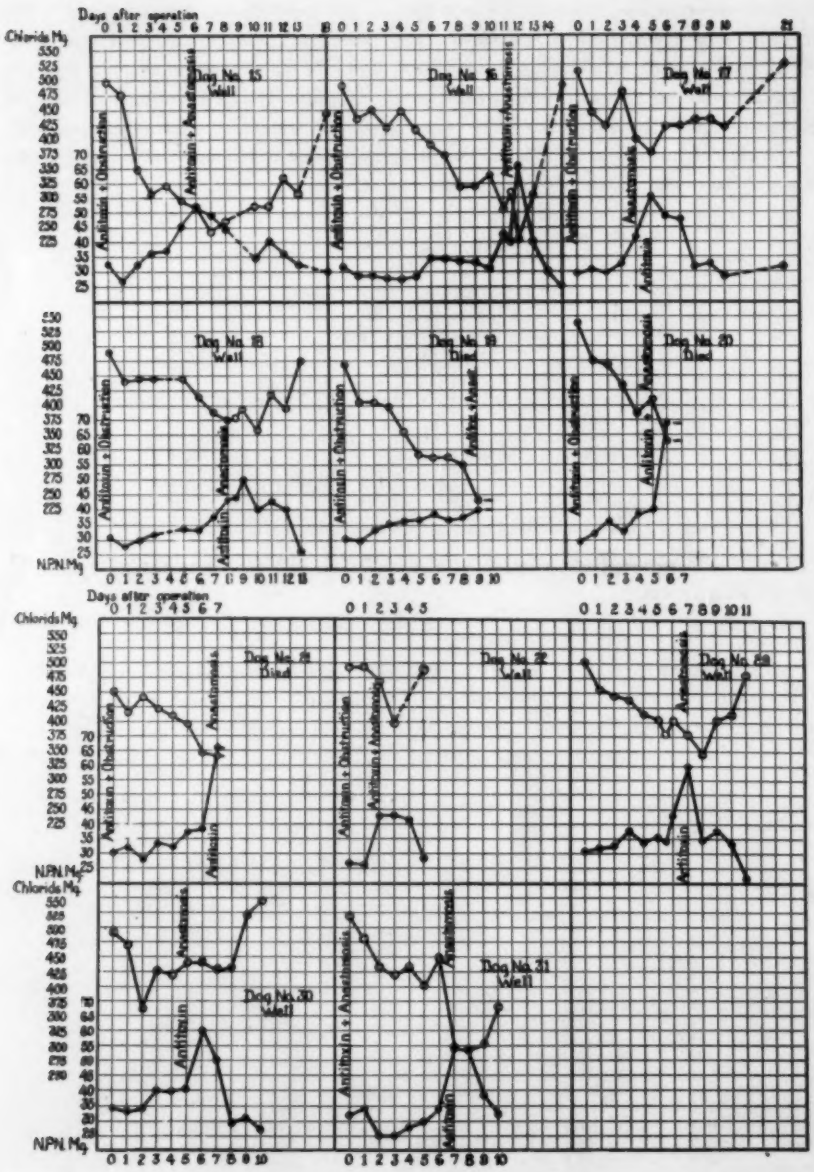

Chart 4.—Results of obstruction of the jejunum with lateral anastomosis after toxemia had been established plus the administration of *B. welchii* antitoxin.

TABLE 4.—*Obstruction of Jejunum with Lateral Anastomosis After Toxemia Was Established Plus B. Welchii (Perfringen) Antitoxin*

Dog No.	Day after Operation	Blood, Amount per 100 Cc.		Comment
		Total Nonprotein Nitrogen, Mg.	Chlorides, Mg.	
15	0	32.2	498	Antitoxin, 20 cc.; obstruction
	1	26.5	475	
	2	32.4	350	
	3	36.3	307	
	4	37.0	322	
	5	45.4	296	
	6	51.8	283	Antitoxin, 20 cc.; lateral anastomosis
	7	49.2	243	
	8	44.8	260	
	9	....	...	
	10	34.7	286	
	11	40.5	285	
	12	36.1	333	
	13	32.4	307	Well
	14	....	...	
	18	30.0	445	
16	0	31.5	490	Antitoxin, 18 cc.; obstruction
	1	28.6	435	
	2	28.6	450	
	3	27.9	420	
	4	27.5	450	
	5	28.6	415	
	6	34.3	391	
	7	34.3	373	
	8	33.3	320	
	9	33.0	320	
	10	31.1	338	
	11	42.8	278	
	11½	40.0	310	Antitoxin, 15 cc.; lateral anastomosis
	12	66.0	230	
	13	40.3	304	
	14	30.0	...	
	15	25.0	492	Well
17	0	29.2	515	Antitoxin, 18 cc.; obstruction
	1	30.7	445	
	2	29.7	422	
	3	32.4	480	
	4	42.0	400	Lateral anastomosis
	5	55.6	376	Antitoxin, 15 cc.
	6	48.7	421	
	7	47.2	421	
	8	31.6	433	
	9	32.8	438	
	10	28.5	421	Well
	21	31.7	526	
18	0	30.8	490	Antitoxin, 20 cc.; obstruction
	1	28.0	440	
	2	30.0	445	
	3	31.0	445	
	4	....	...	
	5	33.7	445	
	6	33.3	415	
	7	37.5	390	
	8	43.2	375	Antitoxin, 12 cc.; lateral anastomosis
	8½	44.0	379	
	9	50.0	398	
	10	40.0	357	
	11	42.8	420	
	12	40.0	395	
	13	26.0	475	Well
19	0	30.4	468	Antitoxin, 12 cc.; obstruction
	1	30.0	405	
	2	33.4	405	
	3	35.3	398	
	4	36.4	353	
	5	30.7	317	
	6	38.7	312	
	7	36.8	312	
	8	37.5	300	
	9	40.0	241	Antitoxin, 15 cc.; lateral anastomosis
	10	....	...	Died

TABLE 4.—*Obstruction of Jejunum with Lateral Anastomosis After Toxemia Was Established Plus B. Welchii (Perfringen) Antitoxin—Continued*

Dog No.	Day after Operation	Blood, Amount per 100 Cc.		Comment
		Total Nonprotein Nitrogen, Mg.	Chlorides, Mg.	
20	0	29.4	538	Antitoxin, 15 cc.; obstruction
	1	32.1	475	
	2	36.3	468	
	3	33.0	433	
	4	38.5	386	
	5	40.0	410	Antitoxin, 15 cc.; lateral anastomosis
	6	69.0	340	
	7	....	...	Died
21	0	30.0	450	Antitoxin, 15 cc.; obstruction
	1	32.1	415	
	2	28.6	442	
	3	33.3	422	
	4	32.4	410	
	5	37.5	394	
	6	38.2	347	
	7	66.6	342	Antitoxin, 15 cc.; lateral anastomosis
	7½	....	...	Died
22	0	26.4	492	Antitoxin, 12 cc.; obstruction
	1	26:1	492	
	2	42.8	468	Antitoxin, 12 cc.; lateral anastomosis
	3	43.0	396	
	4	41.4	...	
	5	28.0	490	Well
29	0	30.8	502	
	1	31.6	456	
	2	32.4	445	
	3	37.5	439	
	4	33.3	414	
	5	35.3	403	
	5½	33.5	379	
	6	42.5	408	
	7	60.0	379	Antitoxin, 20 cc.; lateral anastomosis
	8	34.3	344	
	9	37.5	403	
	10	32.4	415	
	11	21.4	481	Well
30	0	34.3	492	
	1	33.3	470	
	2	34.3	362	
	3	40.0	427	
	4	39.5	420	
	5	40.5	439	Antitoxin, 15 cc.; lateral anastomosis
	6	60.0	439	
	7	50.0	427	
	8	29.3	433	
	9	30.8	522	
	10	26.9	545	Well
31	0	31.9	519	Antitoxin, 20 cc.; lateral anastomosis
	1	34.3	481	
	2	25.0	433	
	3	25.0	420	
	4	27.9	433	
	5	30.0	402	
	6	33.9	450	
	7	53.6	296	Antitoxin, 20 cc.; lateral anastomosis
	8	53.0	290	
	9	38.7	304	
	10	32.4	364	Well

Obstructions were produced in six dogs in the usual manner after they had received intravenously other forms of antitoxin and normal horse serum (chart 5, table 5). This experiment was performed to determine whether there was a specific serum reaction. It was necessary to rule out the foreign serum as a factor and perhaps other constituents. Five of the animals died in spite of lateral anastomosis and antitoxic serum. Neither the horse serum itself, the specific antitoxins for diphtheria or tetanus nor antimeningococcus serum seemed to be effective in preventing death from toxemia.

SUMMARY

Dogs in which obstructions are produced by dividing the jejunum and turning in the loops 10 inches below Treitz's ligament die in from three to ten days.

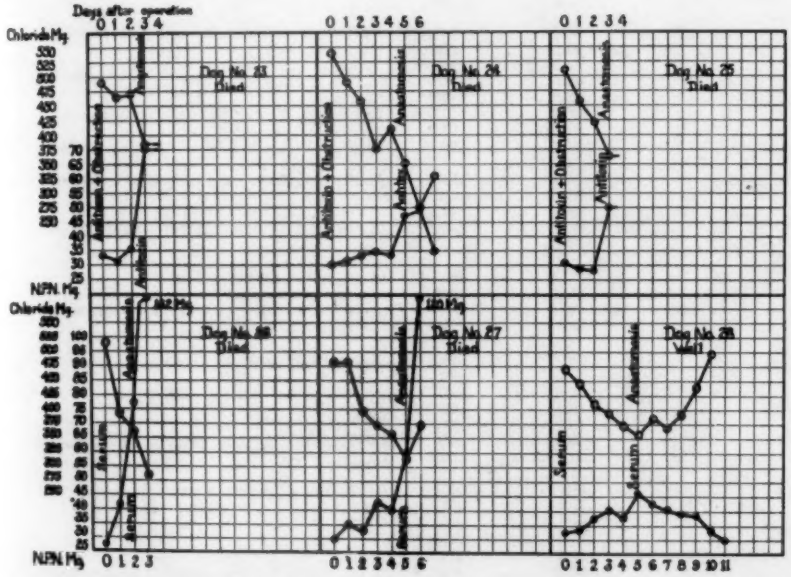

Chart 5.—Results of obstruction of the jejunum with lateral anastomosis after toxemia had been established plus the administration of nonspecific antitoxin.

These animals show a toxemia manifested by clinical signs and by changes in the blood chemistry.

Dogs in which the obstructions have been present until a well marked toxemia develops do not recover even when operation is performed to relieve them from the obstructions.

Dogs in which the obstructions have been present until a well marked toxemia develops may recover when operation is performed to remove the obstruction if *B. welchii* antitoxin is administered intravenously.

The appearance of toxic symptoms seems to be delayed in dogs with obstructions when *B. welchii* antitoxin has been injected intra-

venously; these dogs possibly survive longer than untreated animals under similar conditions.

Dogs in which obstructions have been present until a well marked toxemia develops do not recover when operation is performed to relieve

TABLE 5.—*Obstruction of the Jejunum with Lateral Anastomosis After Toxemia Was Established Plus Nonspecific Antitoxin*

		Blood, Amount per 100 Cc.		
Dog No.	Day after Operation	Total Nonprotein Nitrogen, Mg.	Chlorides, Mg.	Comment
23	0	33.3	490	Antitoxin diphtheria, 30 cc.; obstruction
	1	31.6	465	
	2	35.5	470	
	3	70.0	382	Antitoxin, 30 cc.; lateral anastomosis
	4	....	...	
24	0	30.0	540	Antitoxin tetanus, 20 cc.; obstruction
	1	31.5	490	
	2	33.3	457	
	3	34.5	375	
	4	33.3	410	
	5	47.2	351	Antitoxin, 20 cc.; lateral anastomosis
	6	48.8	272	
	7	34.9	328	Died
25	0	30.8	510	Antitoxin, 15 cc.; meningococcus obstruction
	1	28.6	456	
	2	28.2	421	
	3	50.0	363	Antitoxin, 15 cc.; lateral anastomasis
	3½	....	...	Died
26	0	27.3	515	15 cc. horse serum given
	1	41.3	391	
	2	77.0	300	30 cc. horse serum; lateral anastomosis
	3	162.0	284	Died in ten hours
27	0	30.0	481	15 cc. horse serum given
	1	35.2	461	
	2	33.0	397	
	3	42.8	372	
	4	40.0	355	
	5	60.0	314	30 cc. horse serum; lateral anastomosis
	6	120.0	373	Died
28	0	32.7	469	20 cc. horse serum given
	1	33.7	445	
	2	37.5	408	
	3	40.5	392	
	4	37.5	373	
	5	46.0	355	30 cc. horse serum; lateral anastomosis
	6	42.9	385	
	7	40.5	367	
	8	39.2	391	
	9	38.7	397	
	10	33.3	439	
	11	30.0	497	Well

the obstruction even if antitoxic serums of types other than *B. welchii* have been given intravenously.

CONCLUSIONS

Experimental evidence has been produced to support the contention of Williams that the toxin of *B. welchii* has a bearing on the toxemia of intestinal obstruction.

In a large number of cases, the antitoxin of the *B. welchii* seems to be potent in combination with surgical procedures to relieve the

obstruction in bringing about the recovery of dogs with obstructions. Control dogs do not recover under similar circumstances.

The antitoxin seems to be specific in its action, as other forms of antitoxin and serum are not effective.

These experiments give only indirect evidence that the toxin of *Bacillus welchii* is concerned. Additional experiments on the direct effect of the toxin are being conducted.

A REVIEW OF UROLOGIC SURGERY

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URETHRA

Urethrography.—Miyata and Kajikawa [1] have made forty-four urethrograms in thirty-two cases of normal and pathologic urethras. In some cases material was injected into the bladder and a urethrogram obtained during micturition, and in the others the urethrogram was made during injection of the urethra. They used 40 per cent iodized oil, from 5 to 15 per cent sodium bromide, from 5 to 15 per cent sodium iodide, from 5 to 10 per cent calcium bromide and from 5 to 10 per cent calcium iodide. The 40 per cent iodized oil was found to be satisfactory. The complications in certain cases were intense pain and hematuria, sometimes for two days following injection. The oil, however, did not cause symptoms. Twenty urethrograms are shown and compared to normal cases.

ANESTHESIA

Berry [2] reported 165 consecutive cases of epidural (caudal) anesthesia in perineal operations on the prostate and seminal tract. The series included 140 cases of perineal prostatectomy and 3 of punch operation for benign prostatic hypertrophy, 16 cases of conservative and 3 of radical perineal prostatectomy for carcinoma of the prostate, and 3 cases of radical excision of the entire seminal tract for tuberculosis.

General anesthesia was induced in all cases by a single injection of 20 cc. of a 3 per cent solution of procaine hydrochloride into the extradural space of the sacral canal. Paravertebral injections for blocking the nerves at the sacral foramina on either side, or transsacral

1. Miyata, T., and Kajikawa, H.: Roentgenology of the Male Urethra Especially Posterior Urethra, J. Oriental Med. **6**:31, 1927.

2. Berry, G. P.: Caudal Epidural Anesthesia in Perineal Surgery of the Genito-Urinary Tract, J. A. M. A. **90**:1018 (March 31) 1928.

intradural injections to augment caudal anesthesia, were not used, nor was the extradural injection repeated in case of failure.

Complete abolition of pain following the single injection was secured in 84 per cent of the cases, while in the remaining 16 per cent general anesthesia was required. Serious reactions did not occur, and in 52 per cent of the cases there were no reactions.

Symptoms characteristic of general intoxication from procaine occurred in 10 per cent. The remaining cases showed symptoms secondary to visceral vascular dilatation from paralysis of the sympathetic nerve.

Berry used 20 cc. of 3 per cent solution of procaine and considered that this amount and strength are the most desirable because of absence of any serious reactions.

Young [3] stated that there are several factors to be considered in the choice of anesthetic in prostatic cases. The first of these is the function of the kidneys, as in a large proportion of cases of prostatic hypertrophy there is so much back pressure as to impair renal function. Cardiovascular disorders are also common. In about 3 per cent of the cases the systolic blood pressure was 150 or more. Some form of heart disease was present in almost half of the 198 cases; in many of these, nitrous oxide was distinctly contraindicated.

Young used spinal anesthesia extensively, but has abandoned it because he believed that it is fraught with a certain amount of danger. The region anesthetized is much more extensive than is necessary, and the reactions are dangerous and difficult to counteract. He has used caudal anesthesia since 1924. At first he used a 1 per cent solution, but after a long series of experiments he found that better results and less reaction were obtained by the use of 20 cc. of 3 per cent solution. In a number of cases he was able to carry out his radical operation for carcinoma of the prostate, in which he removed the prostate with the vesical neck, seminal vesicles and ampulla of the vas deferens. The only pain experienced occurred when the vas deferens was reached. To overcome this pain, he now makes a local injection of procaine. There were no operative or anesthetic deaths in 265 cases.

In view of the fact that most of his patients were advanced in years and also that the work of several other men was included, this is an unusual report.

[Ed. Note.—Both Young and Berry stated that they secured the best results when using 20 cc. of 3 per cent solution. The quantity and percentage strength of the solution varies in the hands of different operators. Läwen,[4] who first demonstrated its practicability for

3. Young, H. H.: Epidural Caudal Anesthesia in Prostatic Surgery, J. A. M. A. **90**:1021 (March 31) 1928.

4. Läwen, A.: Die Extraduralanästhesie, Ergebn. d. Chir. u. Orth. **5**:39, 1913.

operative work, recommended from 20 to 25 cc. of 2 per cent solution of procaine with the addition of sodium chloride and sodium bicarbonate. Other formulas have been proposed. It has been maintained that the efficiency of the solution is increased by the addition of calcium chloride, and potassium sulphate has been employed for the same purpose. Meeker and Scholl,[5] in a series of 500 cases, added bicarbonate of soda, sulphate, calcium chloride and a number of other drugs to procaine in an endeavor to increase the efficiency of the anesthesia. Their experience has not indicated that the combination of other solutions with procaine results in more satisfactory anesthesia. In their series of more than 1,800 cases of sacral anesthesia including caudal (sometimes called epidural) and complete intrasacral anesthesia, it was found that 1 per cent solution gave a minimal reaction and the most satisfactory and lasting anesthesia. In a series of 585 cases of simple caudal injections reported by Scholl, the most satisfactory results were obtained with a 2 per cent solution in which approximately 0.6 Gm. of procaine was injected. The percentage of failure following simple caudal injection is greatly reduced by injecting the first and second lateral foramina. This also markedly diminishes the time in which the anesthesia appears.

Caudal anesthesia is not new, but its efficiency is particularly marked in such cases as Young described in which operative approach through the perineum is used. It is also a satisfactory anesthesia for rectal work and for perineorrhaphy. The maximal anesthesia, after caudal anesthesia, is obtained in the space between the rectum and the scrotum and between the rectum and the urethra in the female.]

CYSTOSCOPIC REACTION

Wehrbein[6] reported a series of 328 cystoscopic examinations by three operators with 63 (19.2 per cent) reactions. The operator having the fewest reactions was the one who possessed unusual skill and gentleness in manipulation and exercised good judgment concerning the length of the procedures. On the other hand, reactions occurred more commonly when the operator insisted on complete investigation, although prolonged and difficult, and considered the patient's discomfort less than did the other operators.

Apparently lesions of the urinary tract have nothing to do with cystoscopic reactions. In 279 such cases reactions occurred in 55 (19.7 per cent). In forty-nine cases without lesions of the urinary tract, reactions occurred in eight (16.3 per cent).

The difference between the percentage of reactions due to pyelographic procedures and to mere ureteral manipulations is not great. There were 20.7 per cent reactions with pyelography and 14.3 per cent

5. Meeker, W. R., and Scholl, A. J.: Sacral Nerve Block Anesthesia; the Anatomy Involved, Technic and Clinical Application, Ann. Surg. **80**:739, 1924.

6. Wehrbein, H. L.: Cystoscopy Reactions, Ann. Surg. **87**:435, 1928.

with ureteral manipulations. Five of twelve double pyelograms (41.7 per cent) were followed by reactions. This not only points to the inadvisability of making double pyelograms, but accentuates the fact previously mentioned, that the pyelogram per se represents an additional injury.

Wehrbein concluded that the presence of infectious organisms and trauma are the most significant factors in the causation of reactions following cystoscopy. Elevation of the temperature and injection of the urinary tract, with the exception of acute prostatitis, are not absolute or even common contraindications to cystoscopy.

CHEMISTRY OF THE BLOOD

Bandler and Killian [7] reviewed extensively the value of chemical analysis of the blood in urologic cases. Various methods were discussed and the results of chemical analyses were reported in eleven cases which represent various degrees of renal impairment due to lesions in the urinary tract. The practical value of chemical analysis of the blood was discussed in relation to a determination of the therapeutic measures to be employed. Cases 1 and 2 illustrate the improvement of renal function that follows relief of urinary obstruction and the increase in the volume output of urine caused by forcing fluids. In the second case, failure to relieve the obstruction by catheterization signified the necessity of immediate surgical intervention despite the elevation of the blood urea nitrogen. The preoperative improvement in renal function diminished the surgical risk, and failure to utilize the data obtained in chemical analyses as an index to treatment increased the surgical risk. Increasing the fluid intake did not appreciably influence the retention of nitrogen in the blood unless the urinary obstruction was removed.

In cases showing nitrogen retention, the prognosis, whether from a surgical or medical standpoint, should be based not on the concentration of any one nitrogenous waste product in the blood, but rather on the relative concentration of urea nitrogen and of the creatinine. When the retention of nitrogen in the blood is due to mechanical obstruction, a rise in urea nitrogen and creatinine to the same extent is observed. In chronic renal impairment, however, a relatively greater concentration of creatinine than of the urea nitrogen is noted. Analogous changes in the chemical composition of the blood are observed in cases of mechanical obstruction in the urinary tract, whether this obstruction occurs in the urethra, in the bladder, in the ureters or in the kidneys. The retention of nitrogen observed after obstruction of one ureter is as great as in bilateral ureteral obstruction. This observation has been corroborated by animal experiments.

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7. Bandler, C. G., and Killian, J. A.: The Practical Value of Chemical Analysis of the Blood in Urological Conditions, J. Urol. **19**:1, 1928.

PAIN IN THE BACK

Kutzmann [8] stated that a significant relationship exists between urologic conditions and pain in the back. He discussed the causes of urologic disorders and described the character and nature of the pains involved. In summarizing, he concluded that the genito-urinary tract plays the chief part in the etiology of pain in the back and that the causes of urologic disorders may be divided into four groups: (1) localized or visceral pain, (2) radiating colic-like pain, (3) referred pain and (4) metastatic pain. He expressed the opinion that the physician should acquire certain preliminary or presumptive evidence before resorting to further urologic procedures.

Hinman, in discussing the paper, noted that the stated conditions may be present often without pain, and that pathognomonic pain of intra-abdominal disease is not present. Certain cases are more characteristic, but the typical pain of appendicitis can be simulated by ureteral stone and vice versa; pain in the gallbladder may be reproduced by renal stone. Hinman also stated, in regard to ureteral pain, that when the pain is referred to the testicles from a lesion in the upper part of the ureter, the tunics of the testicle alone are sensitive, whereas in referred pain in the testicle from lesions lower in the ureter, the skin of the scrotum may also be sensitive. Also the spinal segments supplying the bladder, penis and scrotum are often implicated in referred pain.

KIDNEY

Surgical Nephritis.—Tietze [9] stated that renal decapsulation, until recently, was considered an operation for anuria, threatened oliguria or renal hemorrhage; its use in nephritis was thought problematic. Volhard concluded that the fate of the tubules depended on the circulation of the glomeruli, and gave the following classification:

First Chief Group: Primary parenchymal degeneration (not brought about by a disturbance in glomerular circulation): nephrosis and necrosis.

Infectious nephritides: (1) hemorrhagic nephritis, (2) nephritis dolorosa, (3) embolic nephritis in endocarditis, (4) septic interstitial nephritis (accompanying general sepsis) and (5) hematogenous pus in the kidneys.

Second Chief Group: The disturbance of the glomerular circulation functionally, that is, angiospastic, depends on: (1) acute diffuse glomerulonephritis; (2) the kidney in eclampsia and during pregnancy, and (3) incipient lead poisoning of the kidney.

The disturbance of the glomerular circulation organically depends on: (1) the chronic, that is, unhealed glomerulonephritis in its various

8. Kutzmann, A. A.: Back Pain of Urologic Origin, California & West. Med. **27**:208, 1927.

9. Tietze, Alexander: Erfahrungen mit der Nierendekapsulation, Beitr. z. klin. Chir. **139**:88, 1927.

stages of glomerular circulation disturbance, leading to early renal insufficiency (subacute course of extracapillary nephritis); the subchronic course of intracapillary nephritis disguised by the picture of earlier chronic parenchymal nephritis; a third chronic course simulating the picture of chronic interstitial nephritis; (2) renal sclerosis and true contracted kidney, and (3) amyloid kidney.

The success of decapsulation, according to this classification and as performed by Kümmel, was not noted in nephrosis except in unusual cases, and in necrosis the operation was carried out in cases of anuria with poor results.

The more remarkable results were with the infectious nephritides; bleeding ceased, pains disappeared and the infected kidneys recovered.

In the second chief group, the results in cases of anuria, acute nephritis and eclampsia, such as resumption of urinary flow and rapid recovery from renal disease, were phenomenal. There were, however, some failures.

In the really chronic nephritides or organic disturbances of the renal circulation, Volhard did not note a successful result.

Tietze next mentioned the work of Edebohls and Rovsing, both of whom advocated decapsulation on the theory of renewed circulation from the adjacent tissues.

In conclusion, Tietze stated that the operation of decapsulation is still worthy of consideration even though its indications in the foregoing conditions may be limited.

[ED. NOTE.—A number of reports of operation in cases of nephritis have been published recently. Rovsing [10] reported a series of 157 cases, of which 77 were his own. Thus, fifty-three of sixty-two patients with interstitial nephritis were cured following decapsulation; eight were improved and one died. Of fifty-six patients with granular nephritis, twenty-four were cured, twenty-one were improved, two remained the same and nine died. Eight of twenty-four patients with nephrosis were cured, nine were improved, four remained the same and three died. Of nine patients with glomerulonephritis, four were cured, four were improved, and one remained the same. These patients of Rovsing were operated on during a period of thirteen years. The operative procedure carried out in most of his cases was nephrolysis, that is, shelling the kidney out from its capsule of fat and connective tissue. This operation is carried out through a lumbar incision; the kidney is stripped from its fatty capsule; the membrana propria is lifted and incised near the convexity of the kidney and stripped off by means of blunt dissection to the renal hilum.

10. Rovsing, T.: Chirurgische Behandlung der Nephritiden, Verhandl. d. Dän. Med. Ges. **10**:23, 1922-1923.

Kümmell [11] stated that the good effect of decapsulation is probably due to the removal of the fibers of the sympathetic nerve which are severed from the kidney by the removal of the capsule. The establishment of collateral circulation and the formation of a new capsule, which takes place rather readily, can account only in part for the favorable results. Kümmell reviewed the clinical results of his cases of nephritis in which either nephrotomy or decapsulation was carried out. Nine of forty-two cases in which operation was performed were associated with nephritis dolorosa. Nephrotomy was performed in fifteen, nephrectomy in three, and decapsulation in twenty-four cases. Fifteen of the twenty-four patients were dismissed as almost cured, eight as improved, and one died fourteen days after operation from pneumonia.

Quinby [12] reported three cases of decapsulation for various forms of nephritis treated at the Peter Bent Brigham Hospital; one was a case of hemorrhagic nephritis, one of acute tubular nephritis, and one of chronic glomerulonephritis with edema. After bilateral decapsulation the patients were observed carefully with respect to chemical changes in the blood as well as other more general observations; none of them derived any benefit.

Few reports on nephritis have been published in this country, and these, like Quinby's, do not reflect the general optimism of the reports of Rovsing, Kümmell and Damski from European clinics. Apparently this operation is performed frequently in urologic centers in Europe. It offers enough possibilities to be considered at least in certain types of cases in our urologic clinics.]

Renal Stones.—Beer [13] stated that, before considering operative intervention in the treatment of renal stones, it is necessary to know whether or not the patient's kidney is infected, whether it is sufficiently preserved to be of future service, whether the other kidney is able to support life should nephrectomy be necessary, and whether the involved kidney is the only one the patient possesses. In regard to infection, if a renal stone is removed by nephrotomy, sutures passing through such a kidney may lead to secondary widespread infection, so that nephrectomy is necessary later. If the stone is in a solitary kidney, the kidney should be handled carefully and not removed from its normal position, the operation being performed in situ. On the other hand, if functional tests show that the organ is markedly destroyed and full of pus, unless adequate parenchyma is found, nephrectomy may be advisable.

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11. Kümmell, H.: Die chirurgische Behandlung der Nephritis, Ztschr. f. urol. Chir. **17**:27, 1925.

12. Quinby, W. C.: A Note on the Results of Decapsulation of the Kidney for Various Forms of Nephritis, J. Urol. **13**:321, 1925.

13. Beer, Edwin: Points in the Technic of Operative Removal of Kidney Stones, Ann. Surg. **87**:428, 1928.

In Beer's series of 271 cases of renal stone, he found that in 18 per cent the kidneys were so badly destroyed that it was inadvisable to save the organ. In 5 per cent of the cases, either the other kidney was diseased or the stone was in a solitary kidney, so that it was necessary to remove the stone without dislocating the organ. In the remainder of the cases, Beer's choice of operation was pyelotomy or nephrotomy, or a combination of the two. In recent years, pyelotomy has become the more popular type of operation. In Beer's last series of thirty-eight cases, nephrolithotomy was performed in one, nephrectomy in eight, and pyelolithotomy or combined pyelonephrolithotomy in the remainder. Incision into the pelvis spares the parenchyma of the kidney.

Beer exposes the kidney adequately by means of an inverted "S" incision in the lumbar region which begins close to the eleventh rib at the margin of the erector muscle; it then passes obliquely down through the lumbar space between the crest of the ilium and the last rib. Paralleling the last rib, it should extend forward and downward in front of the anterior spine as far as is necessary to get an adequate approach. The kidney being exposed through this incision is gradually liberated from its perinephric fat; adhesions to the upper pole should be carefully ligated before being cut, and then the kidney can usually be completely liberated and dislocated unless there are contraindications to this procedure. This usually permits the operator to raise the organ well up to the muscular or skin plane. After the kidney is exposed in this way, the ureter should be exposed as a routine and a double loop of heavy catgut should be thrown around the ureter to constrict its lumen, which prevents fragments which may break off from the stone or stones slipping into the ureter, and subsequently causing obstruction or symptoms due to the existence of fragments in either the lumbar or the pelvic ureter.

When the kidney is well exposed, most stones can readily be removed by a posterior pyelotomy incision. Abnormal vessels can usually be pushed aside. At times very large and distorted stones can be readily removed through an incision in the renal pelvis.

After a renal stone is removed, Beer washes out the organ with a strong stream of water introduced through a large catheter, so as to clean out any sand or fragments. Beer has not found fluoroscopy of the kidney at the operating table entirely satisfactory. At times small stones have been removed from the kidney directly after the fluoroscopic examination had shown that the kidney did not harbor more calculi. He carries out Quinby's system of taking pictures of the kidney for immediate development. This procedure is carried out in all his cases, except in those with single small stones.

If the pyelotomy approach is impossible, nephrolithotomy may be necessary. If wide nephrotomy is performed, it is well to control the

bleeding from the renal parenchyma. This is done by putting a soft rubber tube about the renal pedicle, crossing the two loops of rubber tube on the anterior surface of the pedicle, and at the crossing placing an artery forceps.

In cases in which the capsule is stripped from the parenchyma in delivering the organ, it is necessary to remember that in performing pyelotomy the reflected capsule, the adherent perinephric fat, the fat surrounding the kidney, and finally the pelvis itself must be cut through before the stone is reached.

After performing pyelolithotomy, it is immaterial whether or not the pelvis is carefully closed by sutures. In some cases the pelvic incision will not leak even though closure is not made; on the other hand, some pelves which have been carefully sutured leak freely.

Hydronephrosis.—The infrequency of dystocia because of a malplaced kidney prompted Idel [14] to report the case of a woman, aged 34, who had had six spontaneous deliveries, the last four years previously. Examination revealed dystocia due to a pelvic tumor which was thought to be an ovarian cyst. Cesarian section was performed. Following delivery, the uterus was repaired and pushed anteriorly. A large cystic tumor was found retroperitoneally occupying the pouch of Douglas. It was the size of a child's head, with a capacity of 2 liters. It was ruptured during removal, with loss of a great deal of blood. The patient died, and necropsy revealed hydronephrosis in a left unilateral fused kidney at the level of the sacrum.

Maximovitsch [15] discussed the question of plastic operations for hydronephrosis and reported 112 cases. Fifty-two of the patients were men and sixty were women. Hydronephrosis was complete in 104 cases and partial in 8 cases. Infection was present in fifty-six cases and was not present in fifty-six.

The cause was stricture, kink, anomaly, tumor, atony, etc., in fifty cases, stones in forty-seven, tuberculosis in five and not determined in ten.

Nephrectomy was performed in sixty-seven cases, nephrostomy in twenty and plastic operations in twenty-four (neostomy in five, plastic operation and straightening of the ureter in ten, and pelvic resection, with plication in nine).

One hundred and three patients recovered, and nine (8.7 per cent) died. The treatment of hydronephrosis may be either conservative or operative. The former consists of pelvic lavage, which may control an inflammatory process and cause some contraction of a dilated pelvis.

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14. Idel, August: Hydronephrose einer dystopen Verschmelzungsniere als Geburtshindernis, Zentralbl. f. Gynäk. **51**:2913, 1927.

15. Maximovitsch, A. S.: Ueber plastische Operationen bei der Hydronephrosis, Ztschr. f. urol. Chir. **23**:383, 1927.

The presence of ureteral stricture should indicate dilatation with bougies. In certain cases operation should not be performed, such as cases of a large, enclosed aseptic hydronephrotic sac of long duration, especially if the removal by changing the intrathoracic pressure would increase the danger of the anesthetic. In the removal of large kidneys, the size of the operative wound and the trauma may cause emboli.

The operative treatment of hydronephrosis may constitute: (1) a procedure which removes the cause of the hydronephrosis and restores renal function, (2) palliative openings into the hydronephrotic sac and (3) nephrectomy.

Plastic operations are employed to eliminate etiologic factors such as strictures, kinks and growths. The methods are various and manifold. Plastic operations on the renal pelvis and ureter are at times satisfactory. Plastic operations necessitate an efficient and careful technic and must be carried out with meticulous care. Sutures and edges of wounds must be carefully handled if successful healing is to be realized. At best, the results of plastic work are problematic even when complications do not occur and the operation has been technically successful. In the experience of Maximovitsch's clinic, lateral anastomosis has been the least successful, as determined by secondary operation or necropsy.

Maximovitsch believed that sufficient time has not been allowed to determine the results which may occur in this field of surgery. According to him, this type of work has a great future, which has not yet been fully developed.

Mathé [16] has made a plea for early relief by conservative operation for hydronephrosis secondary to aberrant renal vessels with movable kidney or kinking of the ureter.

The renal blood vessels are irregular in distribution and present numerous varieties and anomalies. This is explained by the fact that there may be multiple renal arteries and veins with every conceivable type of branching, depending on the selection of the channels from the embryonic periaortic plexus. Retention of a portion of the normal renal vascular relations of the embryo before the ascent of the mesonephros into the renal fossa may occur.

Most of the anomalous vessels do not cause obstructive symptoms and do not require treatment. In a certain percentage of cases, renal mobility may cause the ureter to sag or hang over a fixed support consisting of an aberrant vessel which leads to mechanical factors and causes obstruction and hydronephrosis.

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16. Mathé, C. P.: The Rôle of Aberrant Vessels in the Production of Hydronephrosis, J. Urol. **19**:211, 1928.

Hydronephrosis secondary to aberrant vessels is characterized by intermittent, regular attacks of renal pain occurring over a period of months or years, usually in the young adult.

It occurs most frequently in patients predisposed to movable kidney who present a peculiar form of the body consisting of an elongated thorax, with a small abdominal circumference in which the paravertebral fossa is shallow, cylindrical or funnel-shaped. Because of the rôle played by renal mobility, it is more common in women, on the right side.

The kink in the ureter can be demonstrated by a proper ureteropyelogram in the vertical position. The dilatation of the ureter and pelvis always commences just above the point of obstruction by the vessel. The enlarged kidney can be palpated in about 40 per cent of the cases.

When conservative measures fail to relieve symptoms, surgical intervention should be resorted to. In early cases division of the vessel and suspension of the kidney will suffice. In the more advanced type presenting the narrowing of the ureteropelvic juncture, it is necessary to widen by plastic operation. In badly infected hydronephrotic kidneys and in those presenting advanced destruction, nephrectomy is the treatment of choice.

Good results were obtained from surgical intervention. In a group of eleven patients who received surgical treatment, there was complete relief of symptoms.

It behooves the urologist, internist and general surgeon to recognize the clinical entity of the particular type of movable kidney which, when it descends over an aberrant vessel, causes marked disturbances and symptoms.

Fabian [17] reported a case of carcinoma of the bladder which did not produce any local symptoms except a hemorrhage. The growth occluded the outlet of the right ureter and led to hydronephrosis with pyelitis, which in turn caused ileus. The outlet of the bladder was so narrowed that cystoscopy was impossible. Tumor was felt on rectal examination and was mistaken for prostatitis. On admission to the hospital, symptoms of ileus dominated the picture, but obstruction in the intestine was not found at operation. The true nature of the condition was made clear by the sudden rapid growth of the tumor. The patient, a man, aged 36, died two months after the first appearance of symptoms in the abdomen and the region of the kidney.

Renal Anomalies.—MacKenzie and Hawthorne [18] reported a series of six cases of unilateral renal aplasia. Five of the patients are living,

17. Fabian, K.: Blasenerkrankung mit ileusartigan Erscheinungen, Zentralbl. f. Chir. **54**:983, 1927.

18. MacKenzie, D. W., and Hawthorne, A. B.: Unilateral Renal Aplasia, Surg. Gynec. Obst. **46**:42, 1928.

and the sixth was examined clinically before death. The diseases ranged from complete absence of a kidney in one case to hypoplasia in two others.

Complete absence of the kidney was reported by Anders in about one case in 1,800, and by Motzfeld in one case in 1,000. Many of these patients showed some abnormality in the genital tract. Moore's statistics showed that 75 of 226 patients examined (33 per cent) had congenital defects of the genital organs. The ureter is completely absent in the majority of cases.

The diagnosis of renal aplasia is important to the urologist. The stress of carrying on all the excretory functions is sometimes sufficient to injure the remaining kidney. Nephritis, the formation of calculus or infection is often found. Ballowitz stressed the frequency of calculi in the solitary kidney, while the combined statistics of Ballowitz, Moore and Anders indicate that a greater than the normal percentage of persons with congenital single kidney die from diseases of the kidney. In 42 per cent of Ander's cases, the single kidney showed advanced lesions of chronic nephritis. Apparently the aplastic condition was more common on the left side than on the right. The aplastic kidneys in this series were all functionless.

Caraven [19] cited a case of horseshoe kidney in a Spaniard, aged 37, with acute ileus. For several days he had noticed a painless tumor in the right lower quadrant. An abdominal incision was made and about 1.5 liters of pus were evacuated from immediately underneath the right abdominal wall. Urine was demonstrated in this material, and an ectopic area of hydronephrosis was found and drained. Cystoscopic and roentgen-ray examinations suggested a provisional diagnosis of pelvic horseshoe kidney. The left side was found intact, and the pyonephrotic part of the horseshoe kidney was removed. There was a urinary fistula which closed in twelve days. The patient recovered.

Ruptured Kidney.—Delzell and Harrah [20] reported a series of eleven cases of ruptured kidney, and emphasized the importance of pyelography in the diagnosis and treatment. The hemorrhage following either traumatic or spontaneous rupture of the kidney may result in extensive secondary lesion, usually with marked extravasation and infection. The future economic welfare of the patient is jeopardized.

The authors concluded that : (1) spontaneous rupture of the kidney is rare and occurs only in the presence of lesions; (2) light trauma

19. Caraven, M.: Obstruction intestinale par hydro-pyonéphrose dans un rein en fer à cheval ectopique; néphrostomie transpéritonéale; guérison de l'obstruction: Heminephrectomie secondaire et guérison définitive, Bull. et mém. de la soc. nat. de chir. **53**:905, 1927.

20. Delzell, W. R., and Harrah, F. W.: Eleven Cases of Ruptured Kidney, J. Urol. **19**:131, 1928.

may cause rupture of the kidney if it is in a state of hydraulic tension; (3) most traumatic ruptures heal without surgical intervention, but the patient should be hospitalized and carefully observed until hematuria subsides; (4) most ruptured kidneys which require operation may be saved by palliative operation; nephrectomy is seldom necessary; (5) the symptoms of ruptured kidney are usually definite but may be mistaken for intraperitoneal lesions; (6) cystoscopy usually is not necessary for diagnosis, but should be done occasionally to determine the condition of the injured kidney; (7) pyelography is an aid to accurate diagnosis in selected cases; (8) moderate leukocytosis (13,000 to 18,000) may not indicate infection, but absorption of the blood clot and secondary anemia; (9) it is safer to investigate doubtful cases under regional anesthesia than to treat them expectantly; (10) operative procedure is indicated to prevent exsanguination, extravasation and infection, and (11) the morbidity incident to a ruptured kidney is more dependent on the state of shock and subsequent infection than on the amount of secondary hemorrhage.

Paranephritic Abscess.—Chwalla [21] defined paranephritic abscess as acute suppurative inflammation of the fatty renal capsule or of the renal fascia. Infection takes place either through an embolic metastatic process or by extension from the kidney or adjacent organs. Most authors believe that it originates in a metastatic abscess of the cortex of an otherwise normal kidney. These abscesses can perforate into the loose pararenal tissue, or infection can take place through the lymph channels. Staphylococcus is the organism most frequently found. Trauma plays a part in a number of cases, probably by producing hematoma in the fatty tissue with subsequent infection. It is difficult to determine whether or not the kidney is involved in the paranephritic process. The diagnostic importance of recent staphylococcus infection, such as furuncle, carbuncle, felon or sore throat, is emphasized. In two thirds of the cases, etiologic factors cannot be elicited. Urinalysis does not aid materially in determining concomitant renal involvement. Normal urine suggests primary metastatic paranephritis; urine which is not normal is suggestive of renal abscess. Nevertheless, all urinary conditions, including anuria of the involved side, may be secondarily induced by paranephritic abscess without the participation of the kidney itself.

Chwalla considered exploratory puncture permissible. The most significant disease from a differential diagnostic standpoint is suppurative retrocecal appendicitis. He is opposed to the more radical methods of exposure, and even removal of the kidney itself. Thirty of his thirty-two patients recovered after simple incision and drainage.

21. Chwalla, Rudolf: Zur Klinik des paranephritischen Abscesses, Ztschr. f. urol. Chir. **23**:339, 1927.

Renal Tuberculosis.—Fédoroff [22] stated that renal tuberculosis usually develops from a blood-borne infection. In most cases the diagnosis is not difficult, as it is based on clinical symptoms and examination of the urine. The treatment consists of nephrectomy. Bilateral infection is the only contraindication to nephrectomy. The immediate operative mortality is about 4 per cent, while the late mortality varies from 13 to 29 per cent. From 60 to 70 per cent of patients should be cured.

Salleras and von der Becke [23] stated that of a series of 1,724 patients with urologic lesions, 278 (16.1 per cent) had renal tuberculosis. The percentage varied from 8.8 to 28 in different hospitals. Cases in which there is hematuria are less common than those in which the chief symptoms are in the bladder. Any spontaneous cystitis must be regarded as due to tuberculosis until proved otherwise. The early cases without any bacilli are the most difficult to diagnose; the others are diagnosed readily. Cystoscopy and catheterization are valuable aids. The prognosis is not unfavorable if surgical treatment is applied promptly. The death rate from operation varied from 0 to 50 per cent, the average being from 5 to 10 per cent. Deaths had not occurred immediately following operation for four years, and only one late death had occurred from pulmonary tuberculosis. Some of their cases date back thirteen years. If the case is advanced, three to four years must elapse before cure can be considered.

Orth [24] stated that in cases of extensive tuberculosis in one kidney and toxic nephritis in the other, removal of the tuberculous kidney permits the other to return to normal. If the second kidney is also infected, it does not return to normal. It is always important to study carefully the remaining kidney and to follow the course of the case. In bilateral tuberculosis, surgery is not indicated.

Polycystic Kidney.—Séjournet [25] stated that association of bilateral pyelonephritis with polycystic kidney usually precludes the possibility of operation. He reported one case in which he performed nephrectomy, and at the end of two years the patient is apparently cured. Nephrectomy was performed on account of the increase in size of one kidney. Hemorrhage and infection were not present, but there was increasingly severe pain in this region. The function of the other

22. Fédoroff: Tuberculose Urinaire, J. d'urol. **24**:463, 1927.

23. Salleras, J., and von der Becke, A.: La tuberculosis renal en la República Argentina, Rev. Asoc. méd. argent. **40**:935, 1927.

24. Orth, Oscar: Klinische Erfahrungen bei Tuberkulose der einen und toxischer Nephritis der anderen Niere, Ztschr. f. urol. Chir. **23**:435, 1927.

25. Séjournet, M. P.: Reins polykystiques, Bull. et mém. Soc. de chir. de Par. **19**:654, 1927.

kidney was good, and the patient had just been through a normal pregnancy. The immediate results following operation were satisfactory.

[ED. NOTE.—In this case the kidney was removed because it was thought to contain a tumor. It was found to be polycystic. Almost invariably, in cases of polycystic disease, one kidney is larger than the other. Removal of the larger kidney, while it relieves the pain, discomfort and abdominal distention, is usually followed by an increase in size of the remaining kidney. There is usually such a small amount of combined renal tissue in the two kidneys that it is necessary to be conservative. Rovsing's operation, which consists of puncturing the various cysts, has given the best results of any operation for polycystic kidney. This procedure is conservative and causes only slight trauma to the kidney. It can be repeated on the other kidney if necessary. Rovsing reported excellent results from this operation.]

Renal Tumors.—Stoeckel [26] reported a case of a primipara, aged 33, with a large, right, renal tumor. He saw the patient in the ninth month of pregnancy. The abdominal wall was slightly edematous and the urine scanty. Ureteral catheterization revealed the right ureter to be patent. There was no secretion from the right kidney. He concluded that a closed hydronephrotic sac was present. The patient became progressively worse, as pressure against the diaphragm caused orthopnea and pre-uremic symptoms. One week later, bags were inserted, resulting in spontaneous delivery. The puerperium was normal. On the tenth day, the patient had a coughing spell and then complained that the tumor had burst. Examination showed it to be smaller than previously. There was a rise in pulse and temperature with abdominal distention. Exploratory laparotomy revealed an inoperable tumor in the upper pole of the right kidney. Subsequently, Stoeckel performed a radical operation with complete removal of the tumor. The patient recovered readily from the operation and was well four years later.

Stoeckel expressed the belief that the operation should have been performed earlier. He stated that the risk from nephrectomy is small, and in a case such as this should be carried out as soon as the diagnosis is made. The tumor was grossly cystic. Pathologic study showed it to be a malignant osteo-adenopapilloma destruens, presumably of the kidney.

Lower and Belcher [27] reported the case of a lipoma in the left kidney in a woman aged 52. The patient complained of pain in the abdomen, contraction of the rectum, indigestion and nervousness. A

26. Stoeckel, W.: Maligner Nierentumor (Osteo-Adeno-Papilloma destruens) und Schwangerschaft, Zentralbl. f. Gynäk. **51**:2906, 1927.

27. Lower, W. E., and Belcher, G. W.: Massive Lipoma of the Kidney with Report of a Case, Surg. Gynec. Obst. **45**:1, 1927.

left pyelogram showed deformity strongly suggestive of a new growth. At operation, the kidney was found to contain a large subcapsular, friable, yellow tumor resembling hypernephroma. Pathologic examination showed that the mass weighed 420 Gm. In the middle on the lateral surface of the kidney was a large subcapsular, globular mass which appeared yellow through the capsule. On section, it was fatty and mottled. In view of the tendency of these growths to local recurrence, roentgen-ray treatments were given. The patient was doing well six months later.

True lipomas of the kidney may be distinguished from lipomatous masses around the pelvis, which occur in atrophic disease of the kidney (Virchow) and from the enormous perirenal tumors first described by Salzer. True lipomas arise in two sites, under the surface of the renal capsule and at the hilum. The pelvic lipoma may be an extension from the cortical growth. Lipomas in the kidney are rare. Before the diagnosis is made it should be ascertained by microscopic examination that the suspected growths are not adenomas or suprarenal rests. As a rule the lipomas are small, but five cases have been reported in which they were of considerable size. Degeneration of lipomas or the replacement of normal tissue by lipomatosis secondary to calculus, tuberculosis, inflammatory atrophy or operative trauma is not rare. These fatty masses arise from fat around the pelvis.

The symptoms, as a rule, are pressure, pain or discomfort in the region affected. Hematuria is seldom encountered. Lipomas occur in middle age. The patients in all of the reported cases were women. The diagnosis of tumor may be made by the pyelogram. The only treatment is the removal of the tumor by nephrectomy, which should be followed by roentgen-ray treatment. The tumors are prone to recur, and at each recurrence are more cellular in type, ultimately assuming sarcomatous characteristics. This is the sixth case of true lipoma to be presented and the fourth to be removed by nephrectomy.

[ED. NOTE.—Lower and Belcher [27] called attention to another type of lipoid growth in the region of the kidney. Fatty degeneration, hypernephroma and suprarenal rests are well known, but subcapsular lipoma is indeed a pathologic rarity. The tendency of these fatty tumors to malignant degeneration in the region of the kidney when such masses elsewhere are usually benign is worthy of note. Again, it will be recalled that this is the site of hypernephroma, a much misunderstood tumor of lipoid characteristics. One wonders why lipoid tumors in general in the region of the kidney are so prone to recur, to become malignant and to spread in a way that causes confusion with regard to their classification as sarcomatous (mesothelial) or carcinomatous (epithelial).]

Colston [28] reported an unusual case in which a solitary cyst was found coincidentally with a papillary cystadenoma in the same kidney. The case reported is that of a man, aged 58, who had a three months' history of profuse hematuria. The hematuria was not terminal at any time. General examination did not reveal gross abnormality. Cystoscopic examination showed that the blood was coming from the right kidney. A pyelogram of the right kidney showed a characteristic deformity in the upper calix. A diagnosis of a right renal tumor was made.

At operation, nephrectomy was performed. The specimen showed papillary cystadenoma of the upper pole and a large solitary cyst of the lower pole.

Quinby,[29] on reviewing the end-results of cases of renal tumor in which the patients were treated in the urologic service of the Peter Bent Brigham Hospital, found an unexplained difference between the duration of life after operation and the time when metastasis became apparent. Excluding all cases in which the growth was found to be invasive, as well as those in which lymph nodes about the renal pedicle and aorta were found the seat of secondary deposit, there still lacked evidence on which to base an opinion as to the clinical prognosis. In many cases in which roentgenograms of the lungs and bones have been carefully studied for metastasis before operation and in which the localized character of the tumor as seen at operation gave every hope of cure or at least long freedom from metastasis, death has taken place at a relatively short period after operation.

Of a group of forty-three cases on record at the time this investigation was undertaken, there were thirty-five in which intensive pathologic study was possible.

There is no adequate pathologic criterion on which to base a prognosis on the duration of life after nephrectomy for renal neoplasm. The size of a renal tumor is not a reliable indication of the character in respect to the degree of malignancy. Occasionally, an entirely benign adenoma may become large. Primary ligation of the vascular pedicle by transperitoneal approach is the most logical method of treatment.

[ED. NOTE.—From a review of the case reports as recorded by Quinby, it is found that he does not follow closely the accepted classification laid down by Ewing. Types of cells are frequently recorded as mixed in a given tumor, such as granular, clear, and spindle. Clear polyhedral cell tumors are generally much less malignant than either granular or spindle cell growths. If the tumors described in his reports

28. Colston, J. A. C.: Solitary Cyst and Papillary Cystadenoma Occurring Simultaneously in One Kidney, J. Urol. **19**:285, 1928.

29. Quinby, W. C.: Renal Tumors: A Clinico-Pathological Study, J. Urol. **19**:265, 1928.

as clear celled without any other qualifying description are considered alone, it will be seen that a rather large proportion of his patients are in the group of those reported living.

A number of pathologists believe that the microscopic changes in renal tumors form a fairly accurate basis for an opinion as to prognosis.]

Gottlieb [30] stressed the importance of early and complete examination in cases of suspected renal tumor; such an examination to include urinalysis, cystoscopy, catheterization of ureters, chromocystoscopy, pyelography, pyelography aided by inflation of the renal pelvis, nephroscopy and pyeloscopy. Pyelograms are far more valuable than cystoscopic data. His operative cases have demonstrated the correctness and reliability of anatomic pictures as revealed by pyelograms, which permit a diagnosis of renal neoplasm, polycystic kidney or pelvic papilloma. When the kidney is small, pyelography, after abdominal inflation, gives excellent results. Gottlieb also called attention to the value of nephroscopy and pyeloscopy, a method of examining the patient before a screen in order to determine the dynamics of the kidney, its position, mobility and adherence to the adjacent organs. These data are of importance in determining whether operation can be performed in a given case. Hematuria did not prove to be an early sign in his cases.

Foged [31] reported a case of bilateral renal tumor in a child, aged 2 years, with a normal blood picture and without enlargement of the spleen or lymph nodes. After removal of the right kidney, typical lymphatic leukemia developed. Diffuse infiltration was found in the extirpated kidney. Foged considered bilateral renal tumor the first stage of aleukemic leukosis. His study of cases of renal tumor reported in the literature, in the material from necropsies of Copenhagen hospitals and of this case showed that leukemic disease of the kidney is seldom solitary, usually appears in typical leukosis, and most often in children. Only lymphatic leukosis was encountered. The infiltration is due to an increase in lymphocytes in the disturbed organ. The two kidneys are about equally affected. Macroscopically, the kidney seems hyperplastic; microscopically, universal infiltration without invasion of the renal epithelium is seen. The clinical picture is not characteristic. Foged stated that the bilateral nature of the lesion is an important diagnostic point.

Granulomas.—Braasch and Hurley [32] described granulomas found in the urinary tract as localized areas of hyperplasia of the mucosa and submucosa, apparently resulting from inflammation. These areas

30. Gottlieb, J.: Sur le diagnostic précoce des tumeurs rénales, J. d'urol. **24**: 224, 1927.

31. Foged, J.: Leukemic Tumors of the Kidney, Bibliot. f. Laeger. **119**:1, 1927.

32. Braasch, W. F., and Hurley, M. V.: Granulomas in the Urinary Tract, J. Urol. **18**:595, 1927.

vary from minute patches in the mucosa to papillomatous proliferations. They may cause hematuria or favor persistent infection; when occurring in portions of the urinary tract inaccessible to inspection, they may be easily confused with neoplasms.

Granulomas occurring in the kidney are rarely of much clinical significance except that they may be the cause of hematuria in hydronephrosis, chronic pyelonephritis and nephrolithiasis. Although there are a number of factors which may cause hematuria in hydronephrosis, granulomatous areas are occasionally observed in the pelvic mucosa when the hydronephrotic sac is opened. These areas are usually dark red, bleed easily with trauma, and appear to have a low papillomatous structure. More rarely they are present as single or multiple large polypoid growths and, while usually situated at the ureteropelvic juncture, they may be scattered over the entire pelvis.

Microscopic examination will reveal inflammatory hyperplasia of the mucosa and submucosa. Hematuria occurring with chronic pyelonephritis may also result from a similar type of granuloma in the pelvis or ureter. With chronic pyelonephritis, the granulomas may be more marked and the mucosal proliferation more predominant, a condition often called pyelitis granulosa. As a result of chronic irritation from a stone long resident in the pelvis, granulomas may be observed in the pelvic mucosa.

Chronic infection in the ureteral mucosa, as in the pelvic mucosa, may produce similar lesions confined usually to one or two areas. Although rarely as generalized as ureteritis cystica, granulomas have, on occasion, been observed scattered over the entire ureter. When localized and occurring near the ureterovesical juncture, as in two of their cases, they closely simulate neoplasm. If a small stone is lodged in the intramural portion of the ureter, granulomas may be often seen protruding from the orifice into the bladder. Neoplasm is at once suggested, but in such cases the possibility of a small stone must be excluded.

Granulomas are usually associated with cystitis. Occasionally, many small areas of acute localized cystitis bearing minute granulomas are observed. The lesions are common in association with chronic cystitis; they may vary from one or two to several areas scattered over the entire bladder, and in these cases they are usually small, low, and without resemblance to neoplasm. This is particularly true of nonspecific cystitis.

The mucosa adjacent to the affected ureteral orifice is a frequent site of granuloma in renal tuberculosis. As this is also a common site of epithelioma, position is not of great diagnostic value. The distinction may be made from the fact that a granuloma will flatten out or largely disappear on full distention of the bladder, a phenomenon which will not occur in the presence of epithelioma. Further differen-

tiation is, of course, possible by the removal of specimens through the cystoscope for microscopic examination. Unfortunately, however, the removal of specimens in this manner cannot always be relied on, since it is not unusual to remove a portion of mucosa adjacent to an epithelioma and get, in consequence, a report of inflammatory tissue. The removal of further specimens will settle the diagnosis. Granulomas occurring with incrusted cystitis are often luxuriant and are then easily confused with neoplasm.

Subsequent to removal of a vesical neoplasm, granulomas are frequently observed and may be difficult to distinguish from early malignant disease. They usually occur in the base and near the internal sphincter, although they may be found in any portion of the bladder. When in the dome in the line of the cystotomy incision, they are particularly difficult to identify. The removal of a vesical neoplasm by the knife is less frequently followed by the formation of a granuloma than when the cautery, diathermy or radium is used. After the latter type of treatment, granulomas may persist for several months.

Granulomas of the urethra associated with gonorrhea are widely recognized and have received adequate attention. They are frequently observed in the urethra in cases of dysuria in women.

Nephropexy.—Petit,[33] after studying the late results in a series of cases of nephropexy performed during the last twelve years, concluded that this operation gives more lasting and better results if it is carried out in cases in which there is renal retention or persistent oliguria. The results are less satisfactory in cases in which nephropexy is performed for pain in the region of the kidney without other urinary trouble.

If patients are having pain from a movable kidney, together with nervous and dyspeptic troubles, signs of renal retention should be ruled out by means of ureteral catheterization.

If the orthopedic or medical treatment does not give the patient relief, nephropexy should be performed because such kidneys usually contain fibrous or perinephritic lesions which diminish their functional value and predispose them to infection.

Radiology.—Gérard [34] quoted several statements of Jeanbreau in regard to examinations of the urinary tract: Patients having pyuria should have a roentgen-ray examination of the entire urinary tract; this should include both kidneys and ureters. Patients having vesical calculi, should also have a roentgen-ray examination of the upper part of the urinary tract.

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33. Petit, M.: Les résultats lointains de la néphropexie, Presse méd. **2**:1365, 1927.

34. Gérard, M.: De l'état actuel des explorations radiologiques dans le diagnostic des affections rénales, L'echo méd. du Nord., 1928, pp. 42-52.

Gérard studied the different means of obtaining satisfactory roentgenographic shadows by the contrast method. He discussed colon insufflation, pneumoperitoneum, opaque ureteral catheters, pyelography and pyeloscopy. He used 30 per cent solutions of sodium iodide for pyeloscopy and 15 per cent for pyelography. Roentgen-ray examinations help in determining the situation, volume, shape, direction and extension of the surface of the kidney, the renal retention and the pelvic motility. In cases of lithiasis it permits precise treatment by indicating the site of the stone.

Perirenal Hematoma.—Meyer and Singer [35] showed that hemorrhage in the region of the kidney collects to form a localized hematoma. They showed that the differentiation of aneurysm of the renal artery and perirenal hematoma is clinically unsound. Conroy found thirty-four cases of aneurysm of the renal artery up to 1923, and Meyer and Singer have found six others. This does not include the cases of periarteritis nodosa, which are more common. Trauma, recent or remote in time and subcutaneous or perforative in type, was an etiologic factor in 50 per cent of these cases of aneurysm. Spontaneous rupture of the renal aneurysm may be due to atheromatous or calcific changes in a sclerotic vessel. In such cases, hypertension alone or hypertension and nephritis are present.

Renal arterial aneurysms are as a rule of the false variety. Periarteritis nodosa shows a predilection for the renal arteries and is characterized by a tendency to produce aneurysms. Syphilis, by producing gummatous arteritis, has been reported as a cause of perirenal hemorrhage. Emboli of the mycotic type may lead to miliary and larger aneurysms of the renal artery, which may subsequently rupture in a manner similar to that occurring in cerebral vessels as a complication of subacute bacterial endocarditis. Low grade suppuration of the renal pedicle appears to be responsible for erosion of the renal artery. In one of their cases, such an erosion led to sacculation and rupture. Jannsen described erosion and aneurysmal dilatation due to a sharp renal calculus. Seven days after the removal of the stone by nephrotomy, perforation of the renal artery occurred.

Conditions causing perirenal hematoma other than that due to renal aneurysms are considered; first there are the diseases of the parenchyma of the kidney such as tumors (hypernephromas, carcinomas, sarcomas and multiple cavernomas), tuberculosis, purulent processes, nephritis, nephrolithiasis, hydronephrosis and polycystic disease. In the latter, the presence of another factor must be considered, namely, abnormal fragility of the blood vessels or a blood dyscrasia.

Primary hemorrhage from the fibrous or fatty capsule of the kidney is next considered. This is comparable to hemorrhagic pachymeningitis

35. Meyer, K. A., and Singer, H. A.: Spontaneous Perirenal Hematoma and Aneurism of the Renal Artery, Surg. Gynec. Obst. **45**:300, 1927.

and is probably inflammatory in origin. It usually follows inflammations in the kidney or its pelvis. It is hemorrhagic perinephritis, and the hemorrhage may be intracapsular or extracapsular.

Morbid processes in retroperitoneal structures other than the kidney and its capsule, such as aneurysm of the abdominal aorta or the ovarian artery, tumors of the suprarenal gland or retroperitoneal tumors, such as angiosarcomas, may likewise lead to perirenal hematoma.

In hemophilia, hemorrhage may arise on rare occasions from the lumbar muscles, but the loss of blood by diapedesis may be alarming.

Diagnostically hematomas of the aneurysmal variety are associated with sudden pain (severe in type and situated in the region of the kidney), hematuria in 50 per cent of the cases, and tumor in the loin. On account of the small caliber of the renal artery, sacculation of it rarely reaches so considerable a size as to give expansive pulsation, thrill, and bruit, the pathognomonic signs of aneurysm. Peritoneal irritation is frequent; reflex vomiting and tympanites are more prominent features.

The symptoms associated with the nonaneurysmal varieties are severe pain, signs of internal hemorrhage, and a rapidly growing retroperitoneal tumor in the loin. Hematuria is rare in contradistinction to its frequency in the aneurysmal groups.

Vogeler reviewed twenty-nine cases up to 1922, and found that only five cases of aneurysm of the renal artery had been diagnosed before death. Likewise, the diagnosis of perirenal hematoma was made only three times up to 1921. The occurrence of severe pain, signs of internal hemorrhage and retroperitoneal tumor enlarging in the loin should suggest perirenal hematoma. Immediate operation is indicated in spite of an operative mortality of about 60 per cent, as conservatism is invariably fatal.

[Ed. Note.—This is a good review of a comparatively rare condition. As Meyer and Singer pointed out, the diagnosis before operation and death is rarely made by any one who has not had previous experience with a case in which the condition was undiagnosed until after death. The experience of Meyer and Singer with four cases has taught them to regard spontaneous perirenal hematoma as an entity demanding immediate surgical intervention. The symptoms of sudden severe pain in the region of the kidney, of signs of internal hemorrhage, and rapidly growing tumor in the loin should be emphasized as the features of a case which should bring this diagnosis up for consideration.]

SUPRARENAL GLANDS

Suprarenal Tumors.—Gibson [36] stated that tumors of the suprarenal glands are comparatively rare; yet the frequent failure to diagnose them

36. Gibson, T. E.: The Diagnosis of Adrenal Tumors with Classification of Adrenal Syndromes and Report of Cases, J. Urol. **18**:33, 1927.

is not so much due to this fact as it is to a lack of appreciation of the three clinical syndromes for which they are responsible. Suprarenal dysfunction may be considered under the terms of hypochromaffinism and hyperchromaffinism as applied to the medulla, and hypo-interenalism and hyperinterenalism as applied to the cortex.

With respect to the cortex, hypofunction is exemplified by the clinical picture of Addison's disease. Hyperfunction of the cortex, occurring in either cortical hyperplasia or neoplasia, manifests itself clinically by characteristic alterations in the sexual sphere and by hypertension. The sexual changes are always toward the adult male type, irrespective of sex.

With respect to the suprarenal medulla, our knowledge of function is as yet too limited to serve as the basis for any known syndrome; yet the tumors of the medulla are in themselves so characteristic that little difficulty should be experienced in their diagnosis in most cases. The three clinical syndromes produced by suprarenal tumors may be considered under the following headings: cortical (carcinoma, or hyperplasia), (*a*) genitosuprarenal syndrome; medullary (neurocytoma, sarcoma), (*a*) Hutchison's syndrome and (*b*) Pepper's syndrome.

Cortical tumors are as common in infants and children as in adults, and are characterized by alterations in the sexual sphere, hypertension and, rarely, pigmentation. Medullary tumors belong distinctly to infancy. In both the Hutchison and the Pepper types the primary growth is generally masked by secondary manifestations; in the former, unilateral exophthalmos is frequently the first and only sign; in the latter, tremendous abdominal enlargement due to metastasis to the liver overshadows all else. These peculiarities render the prognosis in general extremely unfavorable, because the diagnosis, particularly in medullary tumors, is at present based wholly on metastatic phenomena.

Generally, a differential diagnosis of suprarenal tumors and other growths, as well as of cortical and medullary tumors of the gland itself, can be made by the clinical manifestations; yet the added information gained by urologic investigation is often of decided value.

Cortical tumors give rise to the so-called genitosuprarenal syndrome. The symptoms produced exemplify the endocrine activity of the cortex. In the female, sexual alterations are produced which may be expressed by the term "virilism" or "pseudohermaphroditism," and in the male by "precocious puberty." Hypertension is a frequent symptom of diagnostic value in these cases. Pigmentation, such as characterizes Addison's disease, is rarely seen. The Hutchison type of medullary tumor, occurring only in infancy and childhood, is characterized by early orbital metastasis producing unilateral exophthalmos. The primary

growth is usually small and the metastasis is generally the first sign of the disease. The Pepper type of medullary tumor is characterized by rapid abdominal enlargement due to metastasis to the liver. The primary growth is small and the hepatic metastasis is generally the earliest sign of the disease.

The diagnosis is ordinarily easy if these three pictures are remembered, and if the fact is also recognized that most abdominal tumors and enlargements in infants and children are due to either renal or suprarenal tumors. In adults, only 1 of every 200 tumors are renal in origin, whereas in infancy and childhood 1 of every 5 tumors are renal. Probably an even greater proportion are suprarenal in origin. Pyelography is of value in questionable cases.

The prognosis is extremely unfavorable, but the occasional cure following surgical intervention justifies this procedure. Urologic investigation to determine relative renal function is essential preliminary to operation, because it is necessary to remove a kidney with the tumor in a high percentage of cases. At operation, the opposite suprarenal gland should be palpated to determine its presence and whether or not the growth is bilateral.

Gibson, in an analysis of nine representative cases, gave concrete illustrations of the symptoms and diagnostic problems. In only four cases were suprarenal tumors found to be primary and of these one was a cortical tumor in a man aged 57. The systolic blood pressure was 190. The second case was that of a woman, aged 38, with a cortical tumor, who exhibited the typical sexual changes, bearded face, hairy chest, and hypertrophy of the clitoris. The third and fourth cases were both medullary tumors occurring in infants, one of the Hutchison type, the other of the Pepper type. The outcome was rapidly fatal in these four cases. Of the remaining five cases, three were secondary or metastatic growths in the suprarenal gland, and two were considered clinically as probable suprarenal tumors. In the three cases of metastasis, two were of the suprarenal glands, but symptoms pointing to suprarenal involvement were not present. In the third case, squamous cell carcinoma arising in the renal pelvis, had metastasized to the suprarenal glands. Typical symptoms of Addison's disease with pigmentation, asthenia, and low blood pressure characterized this case.

The two remaining cases were considered probable suprarenal tumors, but the diagnosis was not confirmed. One patient was a young man, aged 23, whose symptoms were obesity, marked hypertension, muscular weakness and a peculiar purplish discoloration of the skin. These symptoms were probably on the basis of either cortical hyperplasia or actual cortical tumor of the suprarenal gland. The remaining case was that of a female infant, aged 15 months, whose abdomen was large due to a large liver typical of the Pepper type of suprarenal

tumor. Bilateral pyelography was negative, as was surgical exploration of the right suprarenal gland. Permission for necropsy was not granted, so the diagnosis was not confirmed.

Crosbie and Smith [37] reported the case of a woman, aged 38, who had been normal until the age of 20 when an excess growth of hair appeared on the face and body. At 29, menstruation had ceased. Two weeks prior to admission to the hospital, fever, dysuria, frequency of urination and pyuria developed. A large tumor was found in the right flank. Pyelograms revealed a normal left kidney. The right kidney was on the left side of the median line and below the left kidney; its pelvis and calices pointed downward to the left.

The tumor was removed by operation and was found to be of the suprarenal, cortical cell type. Pyelograms made before the patient left the hospital showed that the right kidney had returned to its normal position with pelvis and calices facing the right side. Normal menstruation was resumed three weeks after the patient's dismissal from the hospital, after a period of nine years of amenorrhea.

The authors discussed the pathology of the suprarenal capsule, with special reference to the two major types of tumor, the medullary neuroblastoma and the cortical cell tumor, which may occur either as a benign adenoma or as a malignant true hypernephroma. The literature was carefully reviewed in detail and cases of other authors recorded.

This case seems to represent the nineteenth authentic case of cortical suprarenal tumor occurring in a female, with the typical changes in the secondary sex characteristics noted in relation to these tumors. It is apparently only the third or fourth case which has occurred in the adult during the child-bearing period, and also is one of the few cases on record in which the diagnosis has been confirmed by operation and a cure effected with reversion to the feminine habitus.

URETER

Ureteral Stone.—Jefferson [38] reported a ureteral stone that measured 83 by 41 mm. (3.25 by 1.63 inches) and weighed 106 Gm.

[Ed. Note.—The stone reported by Jefferson is exceptionally large, especially since such conditions are now discovered in an early stage of the growth. In early reports of urinary calculi large stones were occasionally mentioned. Pozzi reported a stone weighing 34 Gm. and Fédoroff reported one of 52 Gm. The largest stone on record was reported by Carlles. This was in the pelvic ureter, and weighed 803 Gm.]

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37. Crosbie, A. H., and Smith, L. W.: Primary Tumors of the Suprarenal Capsule with Especial Reference to Adrenal Virilism, J. Urol. **19**:241, 1928.

38. Jefferson, J. C.: A Large Ureteral Calculus, Brit. M. J. **1**:14, 1928.

Ureteral Carcinoma.—Carson [39] reported two cases of carcinoma of the prostate with metastasis to the ureter and also a case of primary carcinoma of the prostate with metastasis to the renal pelvis. There is a paucity of literature on this subject. Garceau reviewed thirteen cases of metastatic carcinoma in the ureter due to extension by continuity. Giordano and Bumpus reported a case of carcinoma of the left ureter and renal pelvis which did not show invasion of the lymphatics of the ureter, but they were able to demonstrate cancer cells in the blood vessels of the lungs and in a metastatic renal infarct, and thus to conclude that transmission occurred by way of the blood stream. Thomas and Regnier, in 1924, likewise reported a case of carcinoma of the bladder with metastasis to the lymph nodes, psoas muscle and right ureter, without indicating the path of transmission.

Carson's two cases and those previously reported were noted at necropsy, the patients having died of carcinoma of the prostate. At necropsy, the lymphatics of the ureter were found invaded by cancer cells, the growth involving the ureteral walls.

The lymphatics of the ureter are more numerous in the adventitia and muscular coats. They accompany the arteries and drain in three directions, the lower portion downward in the direction of the bladder, the pelvic and abdominal portions mesially into the pelvic and lumbar lymph nodes, and the upper portion in the direction of the renal lymphatics. Thus, while the lymphatic system is doubtless the earliest and most frequent site of metastatic lesions in carcinoma of the prostate, it seems that the drainage of the lymph downward in the lower portion of the ureter is the explanation of the rarity of metastasis to the ureters from the prostate or other pelvic viscera.

[Ed. Note.—Carcinoma of the cervix and prostate by local infiltration may sometimes cause pressure on the ureter, but, as this study shows, direct lymphatic transmission of the disease to the ureter is not the rule. Carson's cases may present a phase of retrograde extension of malignancy against the lymph stream which may be confusing in the consideration of carcinoma in other organs.]

Key and Akerlund [40] referred to the importance of roentgen-ray examination in the diagnosis of rare ureteral tumors. These are either primary or secondary to renal tumors and are usually epithelial. Fifty-four such cases have been reported by Stewart, and to these Key and Akerlund added two. Symptoms are not characteristic, but with the aid of the roentgen ray many cases can be diagnosed. The usual sign is hematuria, and in 55 per cent of the cases hydronephrosis or hemato-

39. Carson, W. J.: Metastatic Carcinoma in the Ureter: Report of Additional Cases, Ann. Surg. **86**:549, 1927.

40. Key, E., and Akerlund, A.: Ueber die Diagnose der Uretertumoren, Deutsche Ztschr. f. Chir. **200**:428, 1927.

nephrosis. Diagnosis can be made cystoscopically if the tumor extends into the bladder. Occasionally particles of tumorous tissue can be dislodged with the ureteral catheter and recognized as a ureteral tumor. Stone, tuberculosis and ureteral stricture must be ruled out. If the ureteral catheter passes the area of the tumor, there may be a rapid flow of clear urine due to the release of retained urine; if there is also a tumor in the renal pelvis, the flow may be bloody. The ureterogram is the most useful diagnostic aid.

Ureteral Diverticula.—Rathbun [41] reviewed the literature of diverticula of the ureter and added two additional cases to those already noted by Stevens, and also reported one case of his own in detail, thus bringing the number to six cases. Rathbun's patient was a boy, aged 10, with a history of frequent urination since the age of 2. The urine was purulent. On cystoscopy, the ureteral orifices appeared normal, but ureteral catheters curled up in the diverticula just outside the wall of the bladder. A diagnosis of bilateral diverticula of the bladder with ureters opening into them was made. Later, at operation, the diverticula were shown to be of the ureters. The diverticula were excised and the ureters transplanted into the bladder with satisfactory results.

Ureteral Trauma.—Laurent [42] stated that the surgeon should be prepared to repair an injured ureter at any time. There are several types of operations in which ureteral injuries are not uncommon, such as hysterectomy for carcinoma of the cervix, the removal of tumors in the broad ligament and the freeing of inflammatory tumors of the adnexa. When the injury is noticed, an attempt should be made to restore the urinary route by an end-to-end anastomosis if the wound is high, or by vesical implantation if the injury is near the bladder.

There are several methods of caring for the injured ureter. Ureterorrhaphy and ureterocystoneostomy were practiced at one time but are now used only rarely, as the results are unsatisfactory. Ureteral implantation into the intestine following ureteral injury is now practically never done in France. Ureterostomy is indicated when both ureters are injured. Nephrectomy is occasionally performed. This precludes the possibility of later complications such as an ascending infection or hydronephrosis. Laurent favored ligation of the ureter; this is a simple procedure and is much less of a shock to the patient than a nephrectomy would be if an extensive gynecologic operation had already been performed.

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41. Rathbun, N. P.: Bilateral Diverticula of the Ureter: Case Report, J. Urol. **18**:347, 1927.

42. Laurent, P.: De la conduite à tenir en présence des blessures de l'uretère au cours des interventions gynécologiques, Paris chirurg. **19**:212, 1927.

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